R4 + R8 together

L7 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:590812 CAPLUS Full-text
DN 139:133836
TI Preparation of 4-aminoazepan-3-ones as protease inhibitors
IN Marquis, Robert Wells; Ru, Yu; Veber, Daniel Frank; Cummings, Maxwell David; Thompson, Scott Kevin; Yamashita, Dennis Shinji
PA Smithkline Beecham Corporation, USA
SO U.S. Pat. Appl. Publ., 126 pp., Cont.-in-part of U.S. Ser. No. 593,845, abandoned.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003144175	A1	20030731	US 2001-881334	20010614
	WO 2000038687	A1	20000706	WO 1999-US30730	19991221
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1384713	A1	20040128	EP 2003-76211	19991221
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	ZA 2001004208	A	20020523	ZA 2001-4208	20010523
	WO 2002017924	A1	20020307	WO 2001-US27178	20010831
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	AU 2001086983	A5	20020313	AU 2001-86983	20010831
	EP 1320370	A1	20030625	EP 2001-966474	20010831
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	JP 2004509083	T2	20040325	JP 2002-522897	20010831
	US 2004002487	A1	20040101	US 2003-404716	20030401
	US 2005256104	A1	20051117	US 2005-152745	20050614
PRAI	US 1998-113636P	P	19981223		
	US 1999-164581P	P	19991110		
	WO 1999-US30730	A2	19991221		
	US 2000-593845	B2	20000614		
	EP 1999-963112	A3	19991221		
	US 2000-653815	A2	20000901		
	US 2001-881334	A2	20010614		
	WO 2001-US27178	W	20010831		
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OS MARPAT 139:133836
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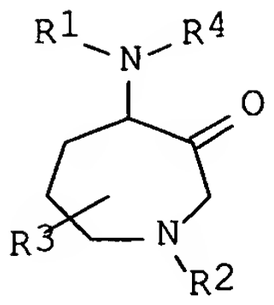

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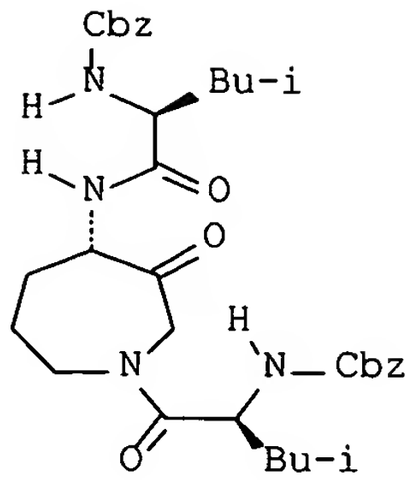


II

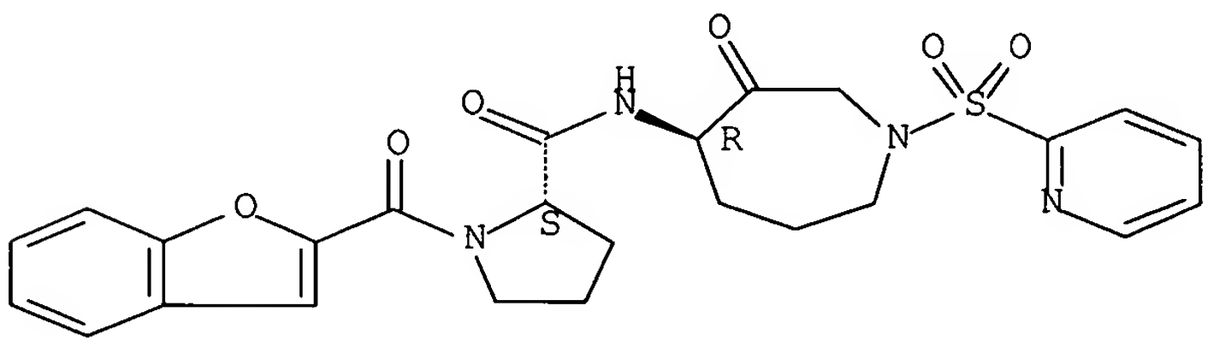
AB Aminoazepanones I [R1 = alkanoyl, amino-, alkoxy-, or alkylthioalkanoyl, etc.; R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, (thio)acyl, alkylsulfonyl, etc.; R3 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, etc.; R4 = H, alkyl, arylalkyl, etc.] or their pharmaceutically-acceptable salts were prepared as protease inhibitors, including cathepsin K, for treating diseases of excessive bone loss or cartilage or matrix degradation, gingival disease, arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease. Thus, compound II (Cbz = benzyloxycarbonyl) was prepared by a multistep procedure.

IT 281216-56-6P 281218-62-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (acylamino)azepanones as protease inhibitors)

RN 281216-56-6 CAPLUS

CN 2-Pyrrolidinecarboxamide, 1-(2-benzofuranylcarbonyl)-N-[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-, (2S)- (9CI) (CA INDEX NAME)

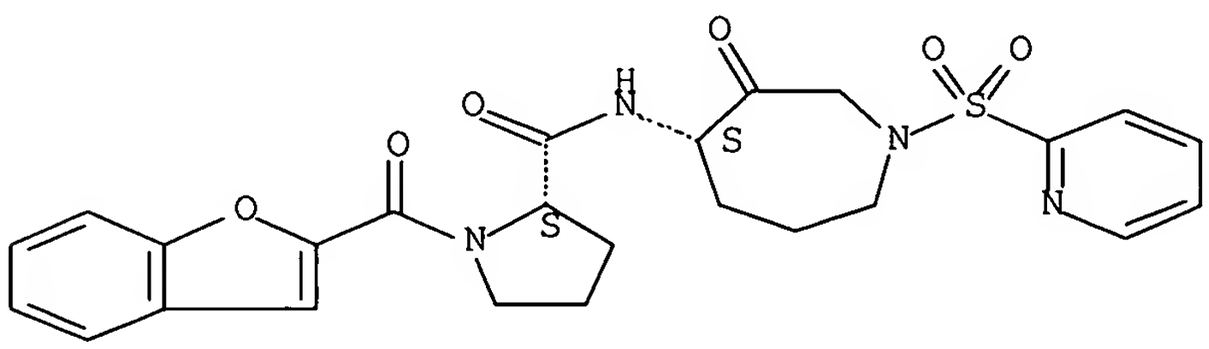
Absolute stereochemistry.



RN 281218-62-0 CAPLUS

CN 2-Pyrrolidinecarboxamide, 1-(2-benzofuranylcarbonyl)-N-[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:888706 CAPLUS Full-text
DN 137:370363
TI Preparation of 4-amino-azepan-3-one derivatives as protease inhibitors
IN Xie, Ren; Yamashita, Dennis S.
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002092563	A2	20021121	WO 2002-US15376	20020515
	WO 2002092563	A3	20030403		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1401453	A2	20040331	EP 2002-744152	20020515
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	US 2004157828	A1	20040812	US 2003-478619	20031117
PRAI	US 2001-291545P	P	20010517		
	US 2001-292646P	P	20010522		
	WO 2002-US15376	W	20020515		

OS MARPAT 137:370363
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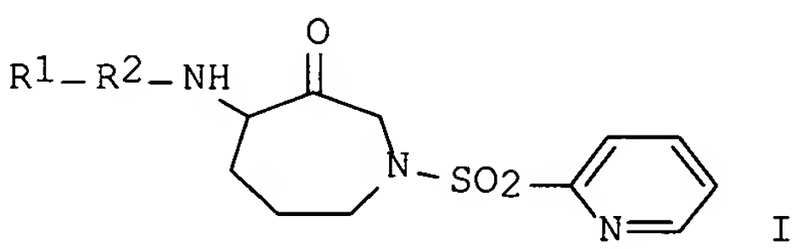

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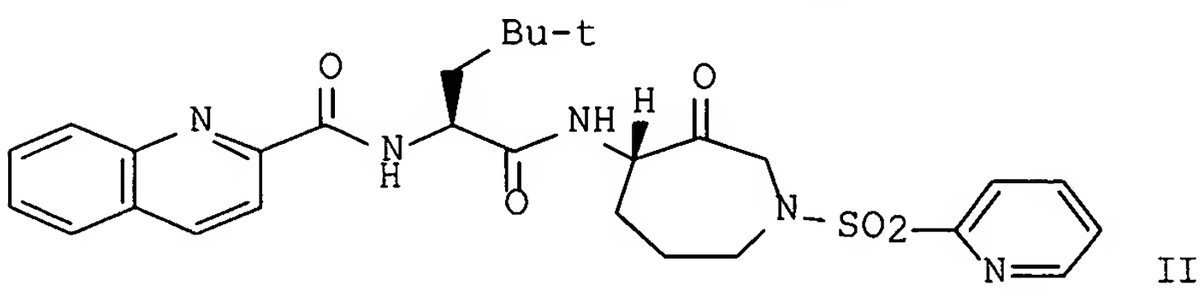


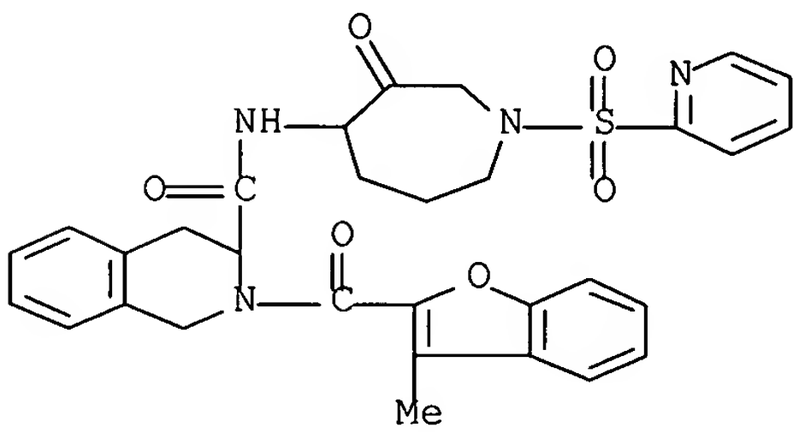
II

AB 4-Aminoazepan-3-one derivs. of formula I [R1 = 3-methylbenzofuran-2- carbonyl, benzofuran-2-carbonyl, 5-methoxybenzofuran-2-carbonyl, benzothiophene-2-carbonyl, quinoline-2-carbonyl, quinoline-3-carbonyl, thiophene-2-carbonyl, thiophene-3-carbonyl, 5-methylthiophene-2-carbonyl, furan-2-carbonyl, furan-3-carbonyl, thieno[3,2-b]thiophene-2-carbonyl; R2 = L-tert-butylalaninyl, L-2-thiophenylalaninyl, L-cyclohexylglycinyl, L-allo-isoleucinyl, tetrahydroisoquinoline-3-carbonyl, L-prolinyl, (S)-2-amino-4-methanesulfonylbutanoyl, (S)-piperidine-2-carbonyl] are prepared which inhibit proteases, including cathepsin K. The compds. are useful for treating diseases of excessive bone loss or cartilage or matrix degradation, including osteoporosis, gingival disease including gingivitis and periodontitis,

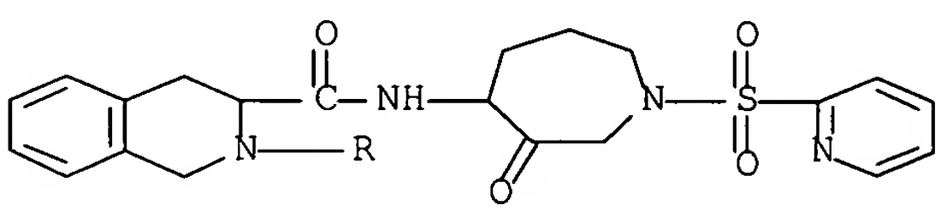
arthritis, more specifically, osteoarthritis and rheumatoid arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease. Thus, II was prepared from 4-amino-3-hydroxyazepane-1- carboxylic acid benzyl ester hydrochloride, 2-pyridinesulfonyl chloride, Boc-L-tert-butylalanine and quinaldic acid. The prepared compds. had Ki values between 2 nM and 1000 nM against cathepsin K in inhibition assays.

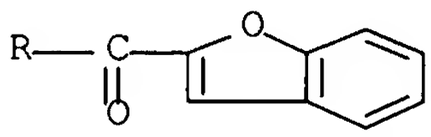
IT 475286-20-5P 475286-21-6P 475286-22-7P
475286-23-8P 475286-24-9P 475286-25-0P
475286-26-1P 475286-27-2P 475286-28-3P
475286-29-4P 475286-30-7P 475286-31-8P
475286-32-9P 475286-33-0P 475286-34-1P
475286-35-2P 475286-36-3P 475286-37-4P
475286-38-5P 475286-39-6P 475286-40-9P
475286-41-0P 475286-42-1P 475286-43-2P
475286-56-7P 475286-57-8P 475286-58-9P
475286-59-0P 475286-60-3P 475286-61-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(preparation of aminoazepanone derivs. as protease inhibitors)

RN 475286-20-5 CAPLUS
CN 3-Isoquinolinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1,2,3,4-tetrahydro-2-[(3-methyl-2-benzofuranyl)carbonyl]- (9CI) (CA INDEX NAME)

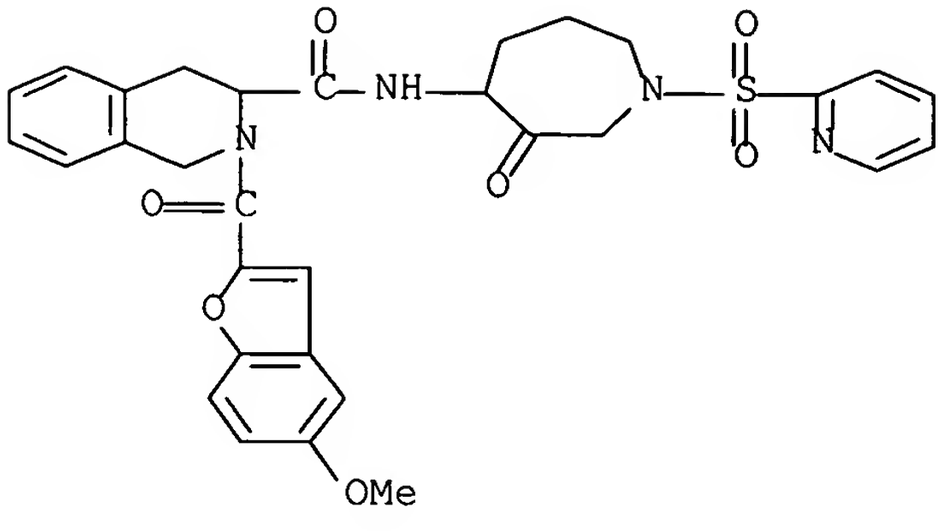


RN 475286-21-6 CAPLUS
CN 3-Isoquinolinecarboxamide, 2-(2-benzofuranylcarbonyl)-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)

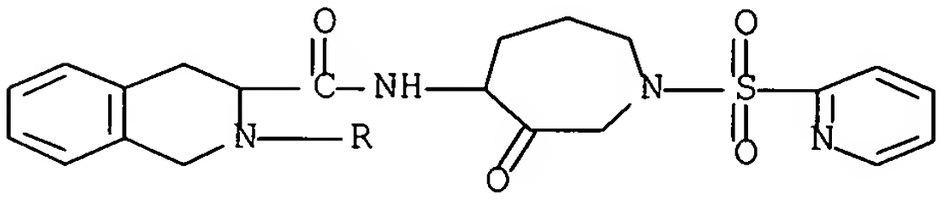


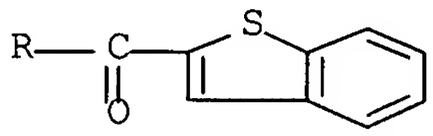


RN 475286-22-7 CAPLUS
CN 3-Isoquinolinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1,2,3,4-tetrahydro-2-[(5-methoxy-2-benzofuranyl)carbonyl]- (9CI) (CA INDEX NAME)

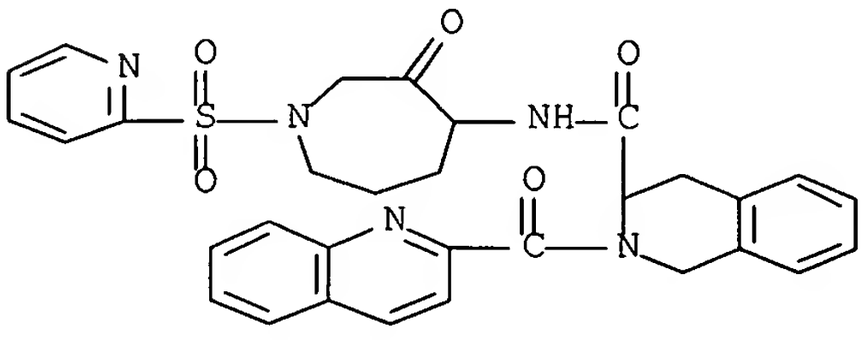


RN 475286-23-8 CAPLUS
CN 3-Isoquinolinecarboxamide, 2-(benzo[b]thien-2-ylcarbonyl)-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)





RN 475286-24-9 CAPLUS
CN 3-Isoquinolinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1,2,3,4-tetrahydro-2-(2-quinolinylcarbonyl)- (9CI) (CA INDEX NAME)



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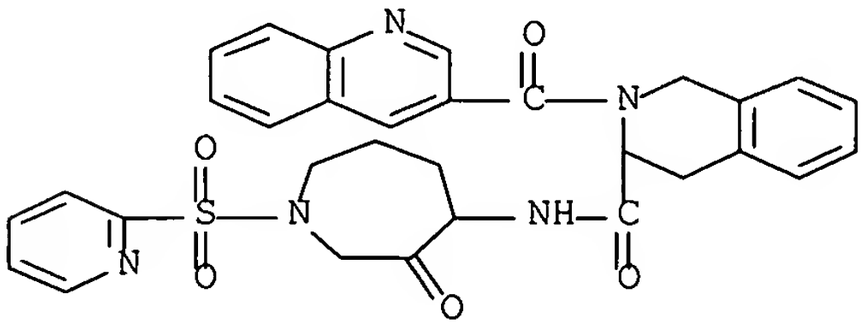
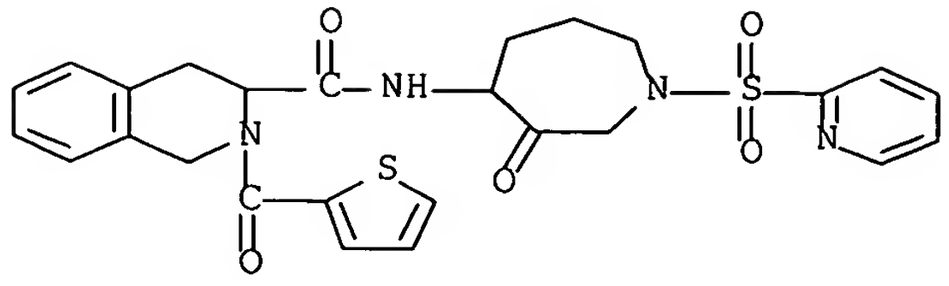
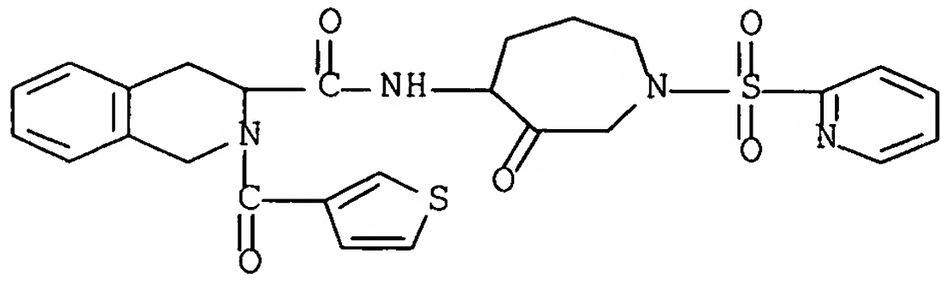
CN 3-Isoquinolinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1,2,3,4-tetrahydro-2-(3-quinolinylcarbonyl)- (9CI) (CA INDEX NAME)



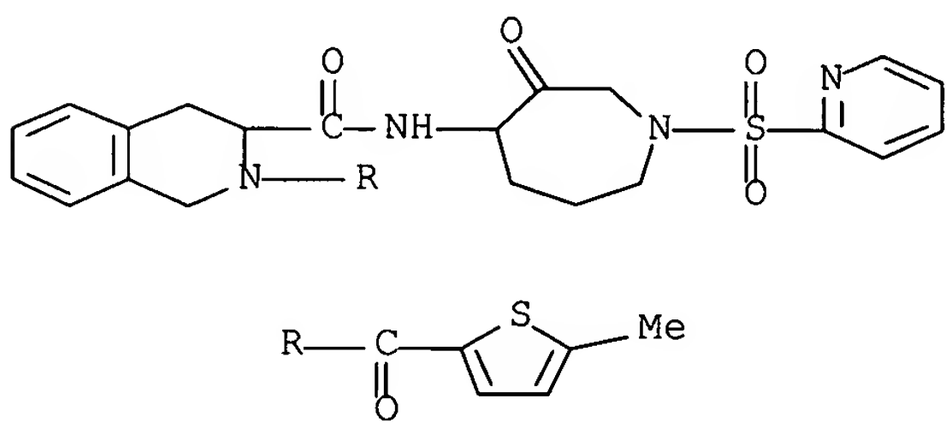
RN 475286-26-1 CAPLUS
CN 3-Isoquinolinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1,2,3,4-tetrahydro-2-(2-thienylcarbonyl)- (9CI) (CA INDEX NAME)



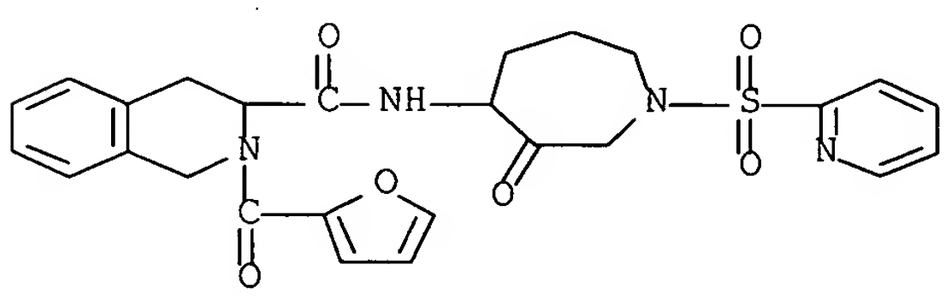
RN 475286-27-2 CAPLUS
CN 3-Isoquinolinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1,2,3,4-tetrahydro-2-(3-thienylcarbonyl)- (9CI) (CA INDEX NAME)



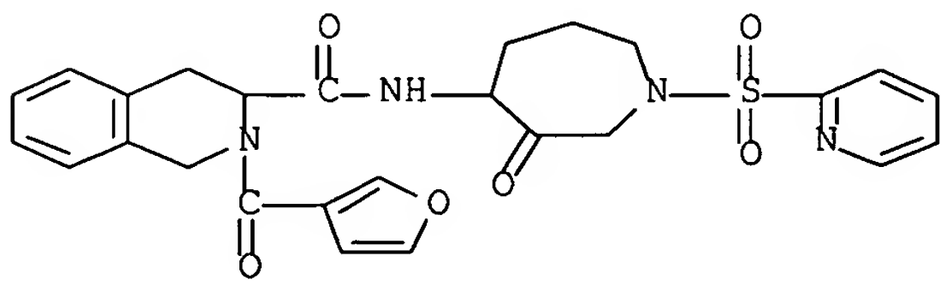
RN 475286-28-3 CAPLUS
CN 3-Isoquinolinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1,2,3,4-tetrahydro-2-[(5-methyl-2-thienyl)carbonyl]- (9CI) (CA INDEX NAME)



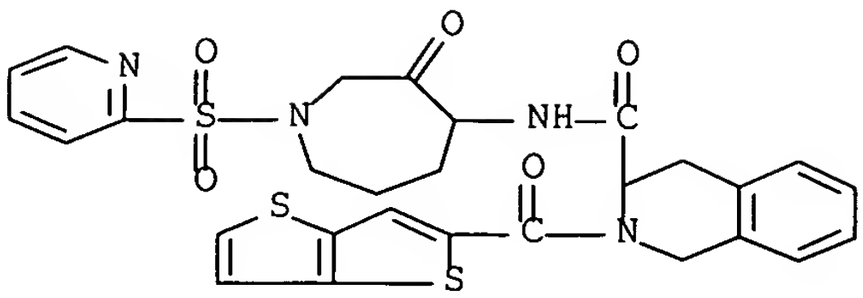
RN 475286-29-4 CAPLUS
CN 3-Isoquinolinecarboxamide, 2-(2-furanylcarbonyl)-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



RN 475286-30-7 CAPLUS
CN 3-Isoquinolinecarboxamide, 2-(3-furanylcarbonyl)-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)

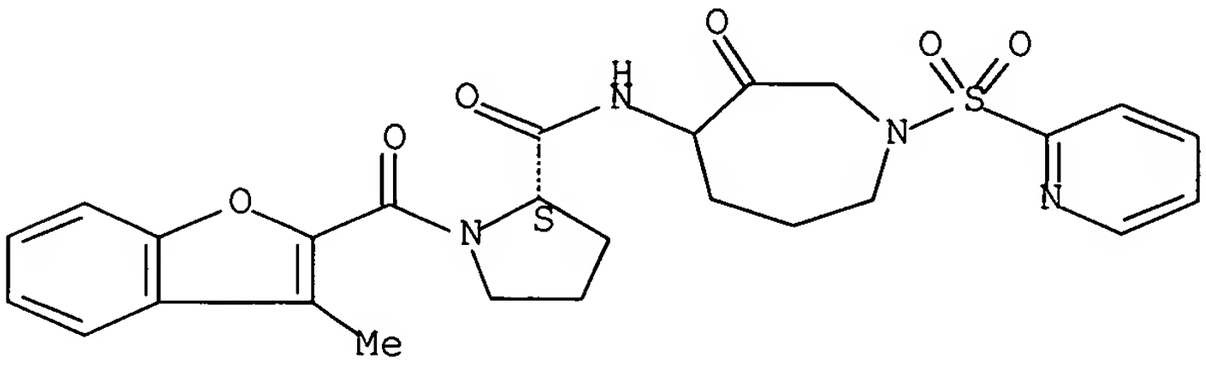


RN 475286-31-8 CAPLUS
CN 3-Isoquinolinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1,2,3,4-tetrahydro-2-(thieno[3,2-b]thien-2-ylcarbonyl)- (9CI) (CA INDEX NAME)



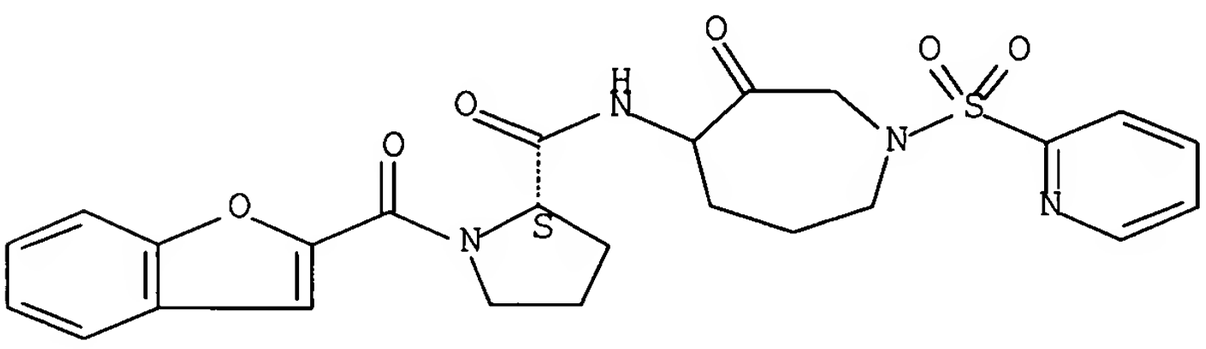
RN 475286-32-9 CAPLUS
CN 2-Pyrrolidinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1-[(3-methyl-2-benzofuranyl)carbonyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



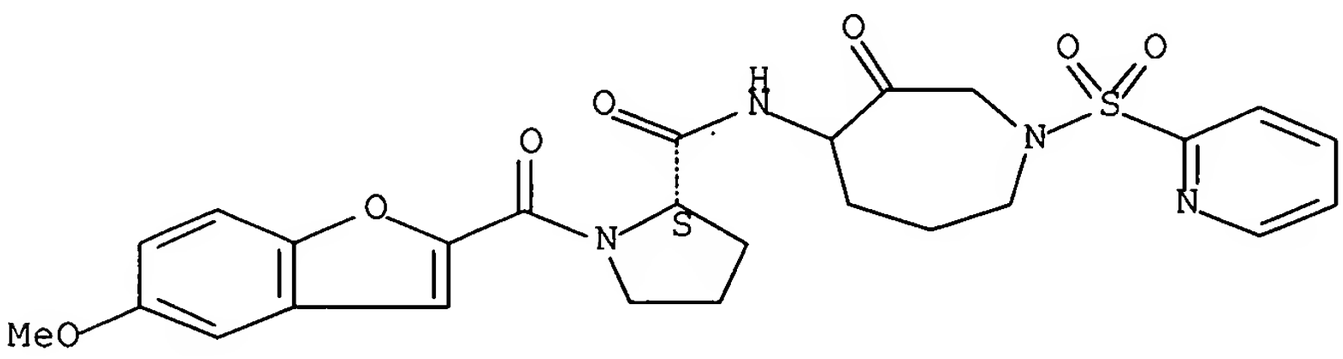
RN 475286-33-0 CAPLUS
CN 2-Pyrrolidinecarboxamide, 1-(2-benzofuranylcarbonyl)-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 475286-34-1 CAPLUS
CN 2-Pyrrolidinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1-[(5-methoxy-2-benzofuranyl)carbonyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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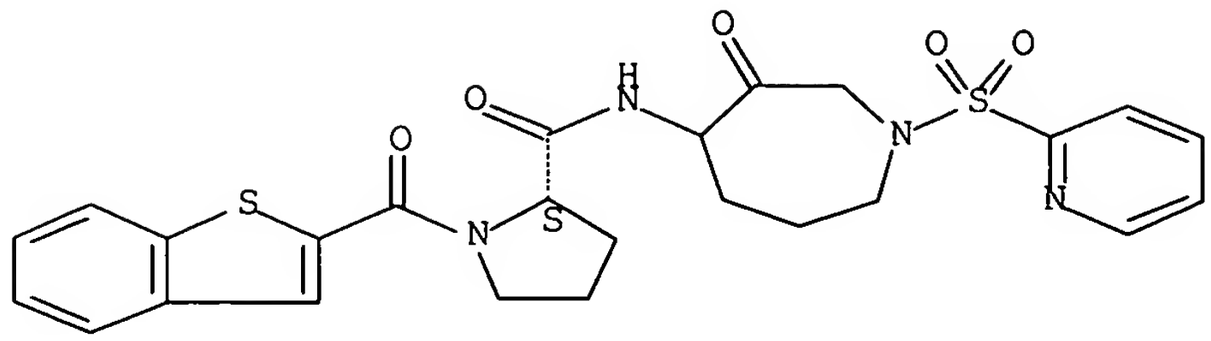
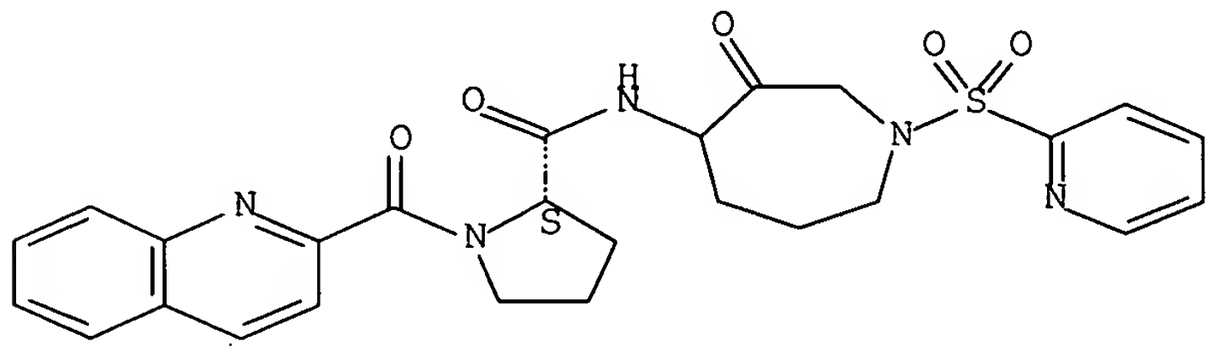
Absolute stereochemistry.



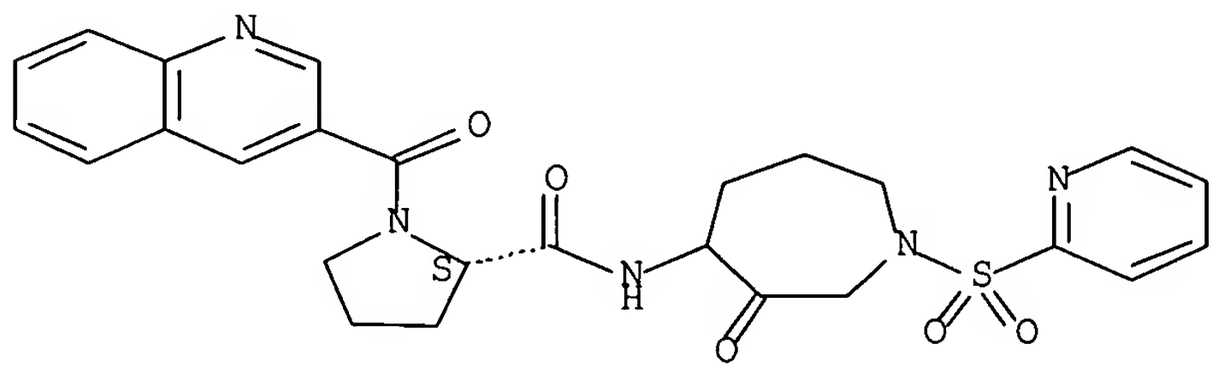
RN 475286-36-3 CAPLUS
CN 2-Pyrrolidinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1-(2-quinolinylcarbonyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



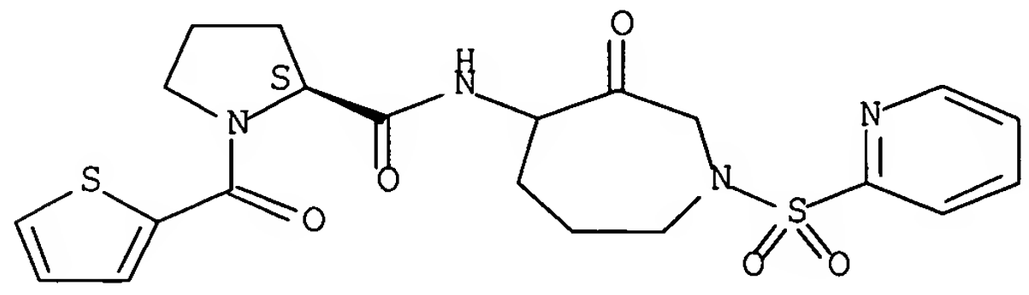
RN 475286-37-4 CAPLUS
CN 2-Pyrrolidinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1-(3-quinolinylcarbonyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



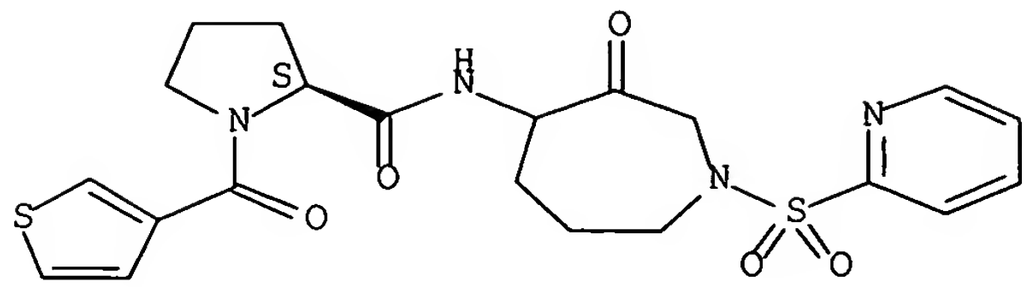
RN 475286-38-5 CAPLUS
CN 2-Pyrrolidinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1-(2-thienylcarbonyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



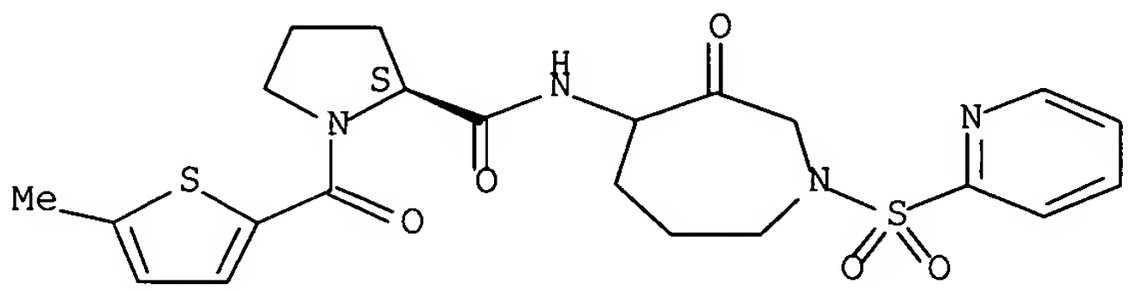
RN 475286-39-6 CAPLUS
CN 2-Pyrrolidinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1-(3-thienylcarbonyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



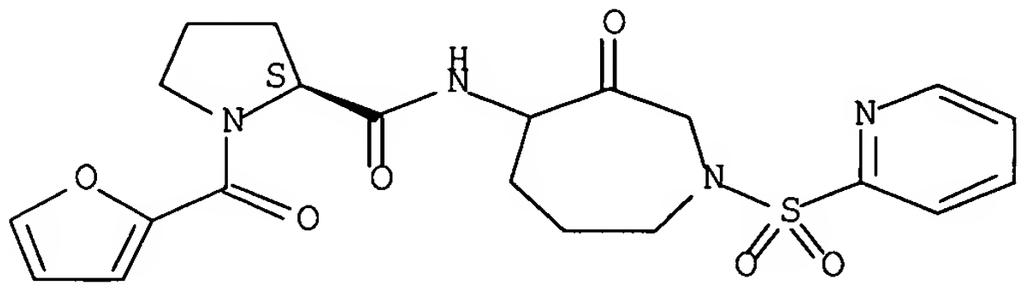
RN 475286-40-9 CAPLUS
CN 2-Pyrrolidinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1-[(5-methyl-2-thienyl)carbonyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



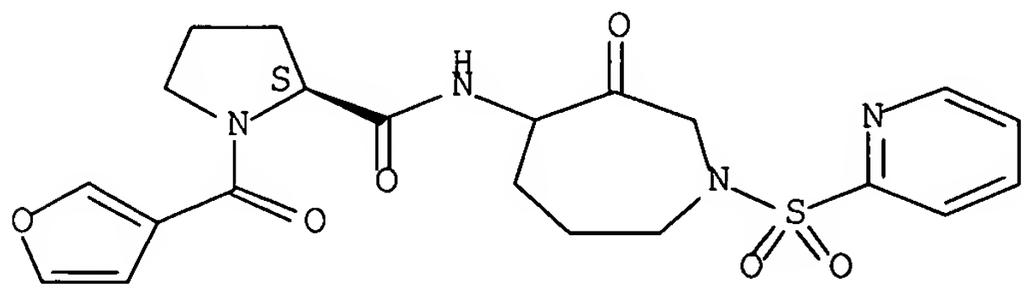
RN 475286-41-0 CAPLUS
CN 2-Pyrrolidinecarboxamide, 1-(2-furanylcarbonyl)-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



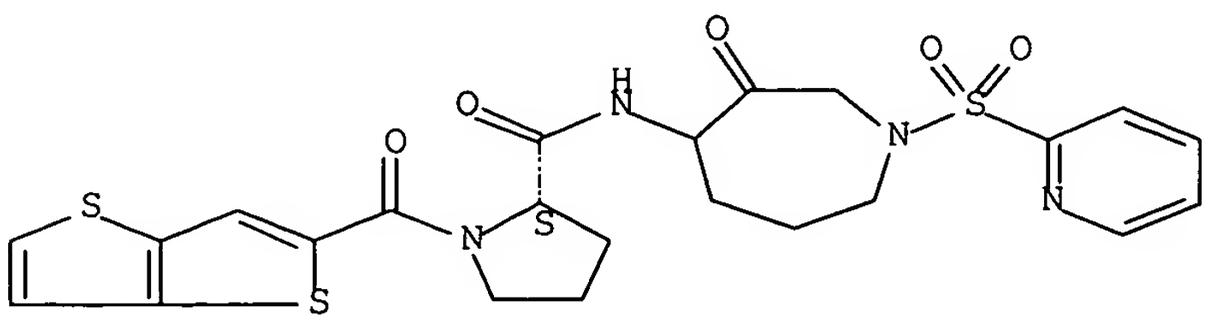
RN 475286-42-1 CAPLUS
CN 2-Pyrrolidinecarboxamide, 1-(3-furanylcarbonyl)-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



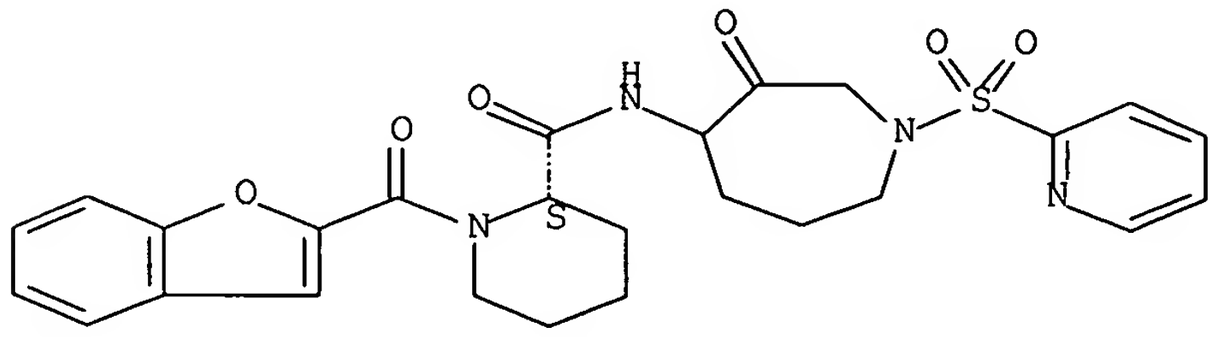
RN 475286-43-2 CAPLUS
CN 2-Pyrrolidinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1-(thieno[3,2-b]thien-2-ylcarbonyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



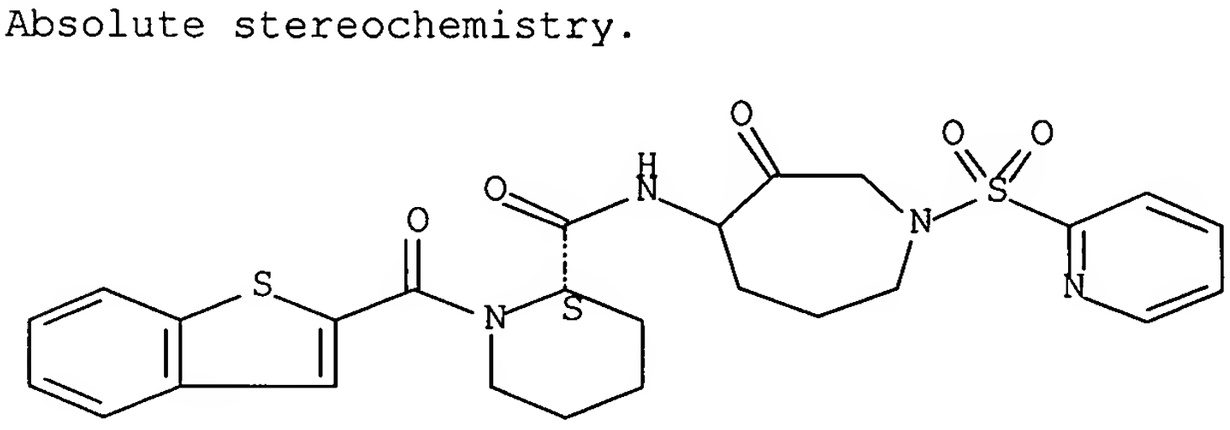
RN 475286-56-7 CAPLUS
CN 2-Piperidinecarboxamide, 1-(2-benzofuranylcarbonyl)-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



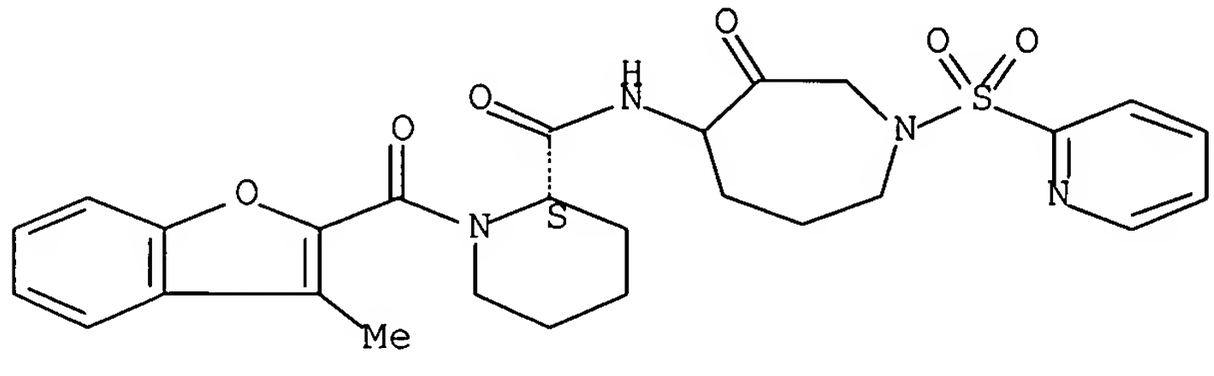
RN 475286-57-8 CAPLUS
CN 2-Piperidinecarboxamide, 1-(benzo[b]thien-2-ylcarbonyl)-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



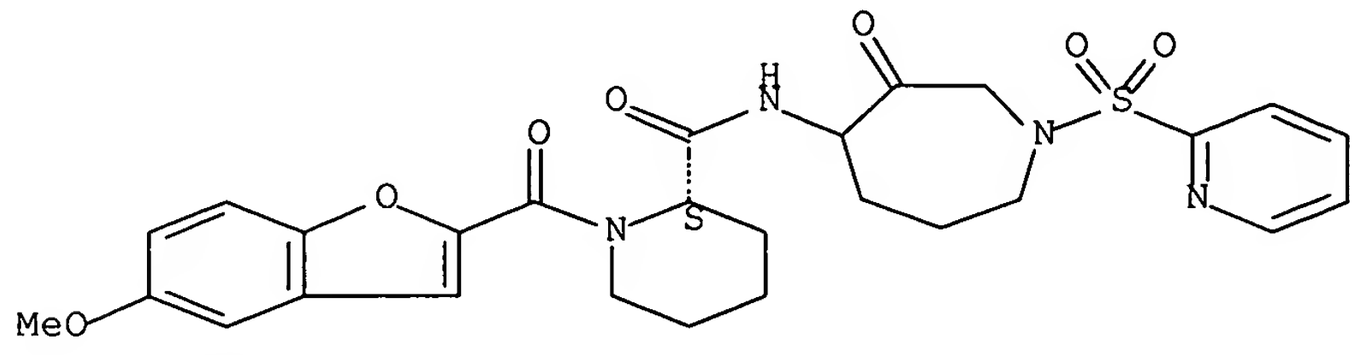
RN 475286-58-9 CAPLUS
CN 2-Piperidinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1-[(3-methyl-2-benzofuranyl)carbonyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



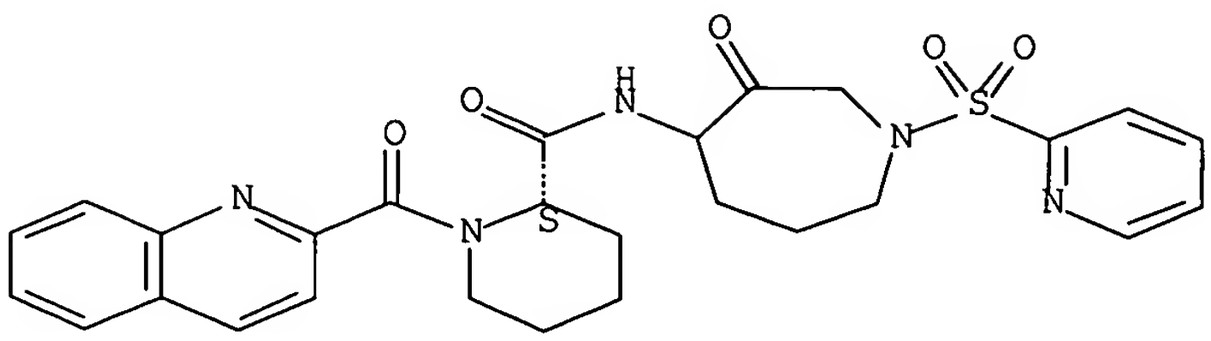
RN 475286-59-0 CAPLUS
CN 2-Piperidinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1-[(5-methoxy-2-benzofuranyl)carbonyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



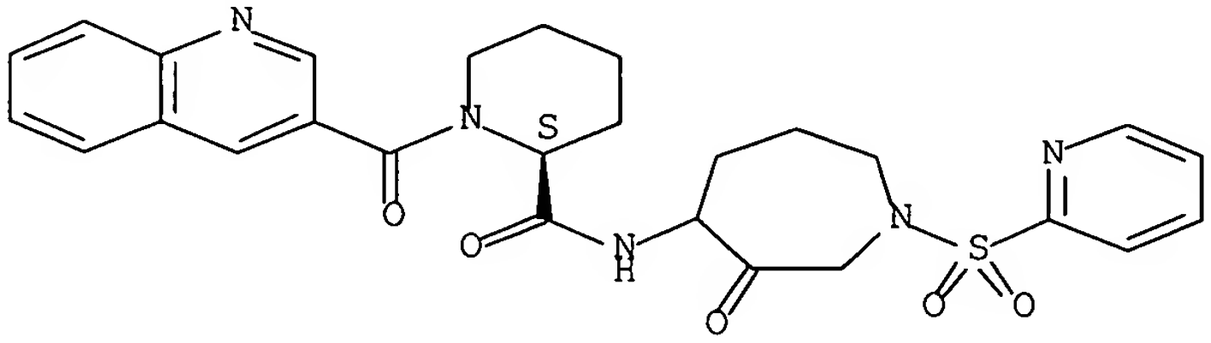
RN 475286-60-3 CAPLUS
CN 2-Piperidinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1-(2-quinolinylcarbonyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 475286-61-4 CAPLUS
CN 2-Piperidinecarboxamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-1-(3-quinolinylcarbonyl)-, (2S)- (9CI) (CA INDEX NAME)

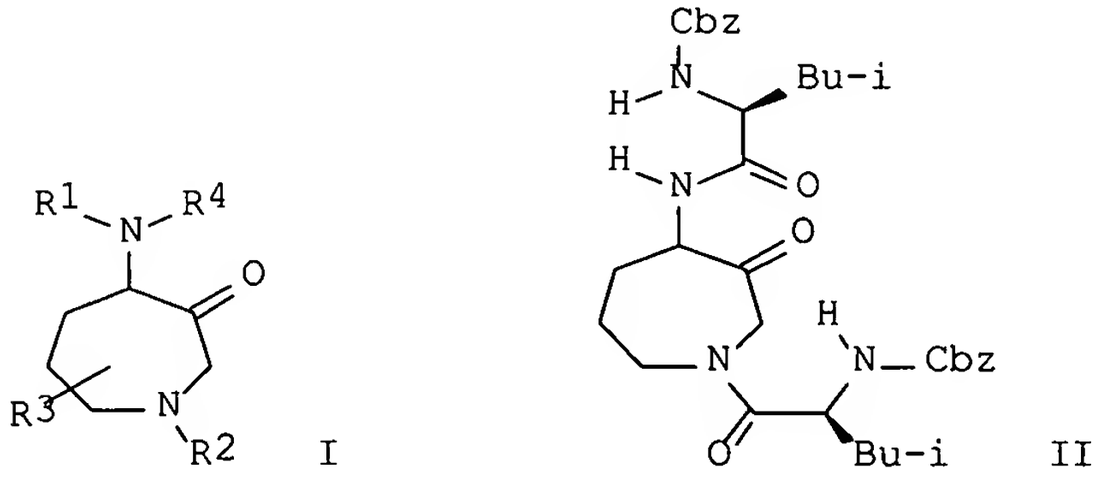
Absolute stereochemistry.



L7 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:923616 CAPLUS Full-text
DN 136:53691
TI Preparation of 4-amino-azepan-3-one protease inhibitors
IN Marquis, Robert W., Jr.; Ru, Yu; Veber, Daniel F.; Cummings, Maxwell D.; Thompson, Scott K.; Yamashita, Dennis
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 322 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001095911	A1	20011220	WO 2001-US19062	20010614
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2412353	AA	20011220	CA 2001-2412353	20010614
	EP 1307204	A1	20030507	EP 2001-946344	20010614
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004503502	T2	20040205	JP 2002-510089	20010614
	BR 2001011693	A	20040406	BR 2001-11693	20010614
	NZ 522965	A	20040625	NZ 2001-522965	20010614
	BG 107327	A	20030731	BG 2002-107327	20021128
	NO 2002005786	A	20030212	NO 2002-5786	20021202
	ZA 2002009808	A	20040709	ZA 2002-9808	20021203
PRAI	US 2000-593845	A2	20000614		
	WO 2001-US19062	W	20010614		

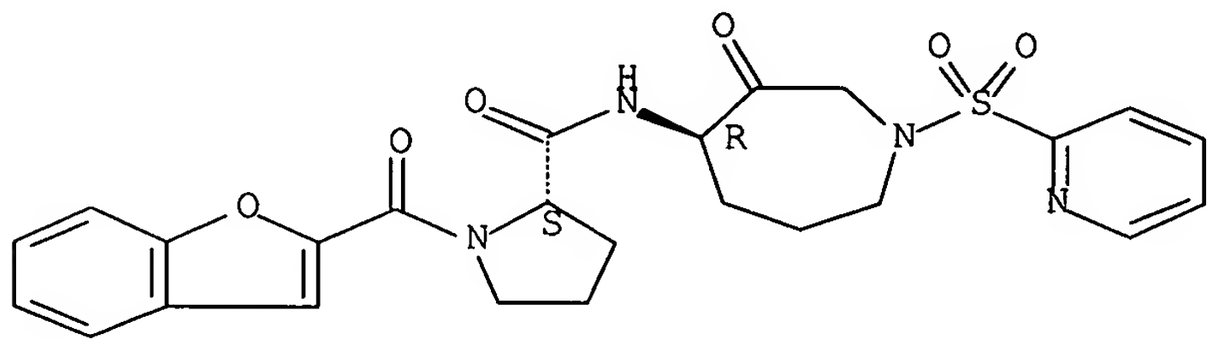
OS MARPAT 136:53691
GI



AB The title compds. [I; R1 = COCR13NR11R12, COCR13XR15, COCH2R13; R2 = H, alkyl, cycloalkylalkyl, etc.; R3 = H, alkyl, cycloalkylalkyl, etc.; R4 = H, alkyl, arylalkyl, etc.; R11 = H, alkyl, arylalkyl, etc.; R12 = H, alkyl, cycloalkyl, etc.; R13 = H, alkyl, alkenyl, etc.; R15 = H, alkyl, alkenyl, etc.] which inhibit proteases (no data), including cathepsin K, and are useful for treating diseases of excessive bone loss or cartilage or matrix degradation including osteoporosis, gingival disease including gingivitis and periodontitis, arthritis, more specifically, osteoarthritis and rheumatoid arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease, were prepared E.g., a multi-step synthesis of compound II was given.

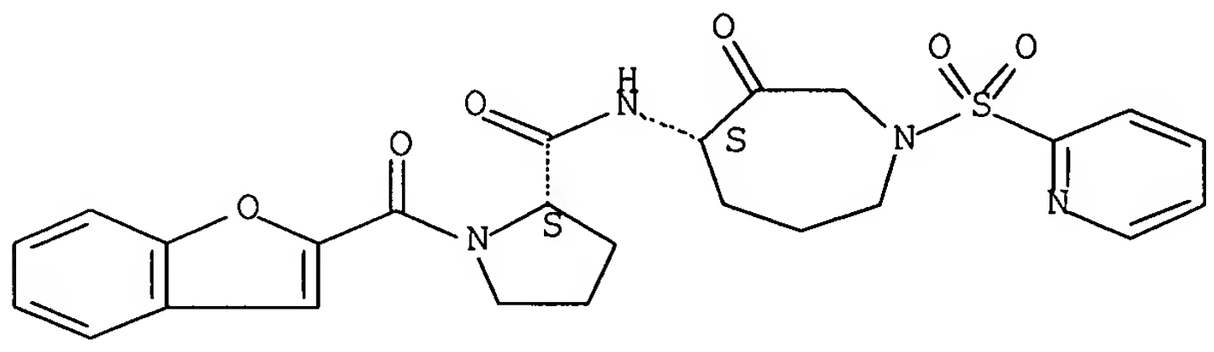
IT 281216-56-6P 281218-62-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(preparation of 4-amino-azepan-3-one protease inhibitors)
RN 281216-56-6 CAPLUS
CN 2-Pyrrolidinecarboxamide, 1-(2-benzofuranylcarbonyl)-N-[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281218-62-0 CAPLUS
CN 2-Pyrrolidinecarboxamide, 1-(2-benzofuranylcarbonyl)-N-[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:456887 CAPLUS Full-text
DN 133:89444
TI Preparation of 4-amino-azepan-3-one protease inhibitors
IN Marquis, Robert Wells, Jr.; Ru, Yu; Veber, Daniel Frank; Cummings, Maxwell David; Thompson, Scott Kevin; Yamashita, Dennis
PA Smithkline Beecham Corp., USA
SO PCT Int. Appl., 273 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000038687	A1	20000706	WO 1999-US30730	19991221
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2356671	AA	20000706	CA 1999-2356671	19991221
	BR 9916488	A	20011009	BR 1999-16488	19991221
	EP 1158986	A1	20011205	EP 1999-963112	19991221
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	TR 200101869	T2	20020121	TR 2001-200101869	19991221
	JP 2002533397	T2	20021008	JP 2000-590640	19991221
	AU 768565	B2	20031218	AU 2000-19411	19991221
	NZ 511710	A	20031219	NZ 1999-511710	19991221
	EP 1384713	A1	20040128	EP 2003-76211	19991221
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	ZA 2001004208	A	20020523	ZA 2001-4208	20010523
	US 2003144175	A1	20030731	US 2001-881334	20010614
	NO 2001003124	A	20010622	NO 2001-3124	20010622
	NO 318910	B1	20050523		
	US 2002147188	A1	20021010	US 2002-74940	20020213
	US 2003044399	A1	20030306	US 2002-74639	20020213
	US 2003225061	A1	20031204	US 2003-404142	20030401
	US 2004002487	A1	20040101	US 2003-404716	20030401
	AU 2003261482	A1	20031204	AU 2003-261482	20031106
	US 2005256104	A1	20051117	US 2005-152745	20050614
PRAI	US 1998-113636P	P	19981223		
	US 1999-164581P	P	19991110		
	AU 2000-19411	A3	19991221		
	EP 1999-963112	A3	19991221		
	WO 1999-US30730	W	19991221		
	US 2000-593845	B2	20000614		
	US 2000-653815	A1	20000901		
	US 2001-881334	A1	20010614		
	US 2002-74940	A1	20020213		
	US 2003-404716	B1	20030401		

OS MARPAT 133:89444
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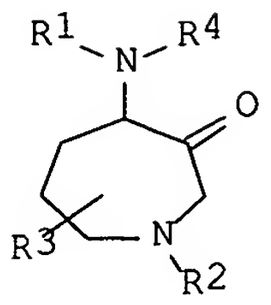

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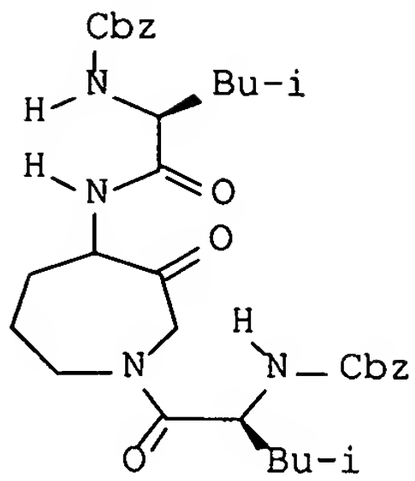


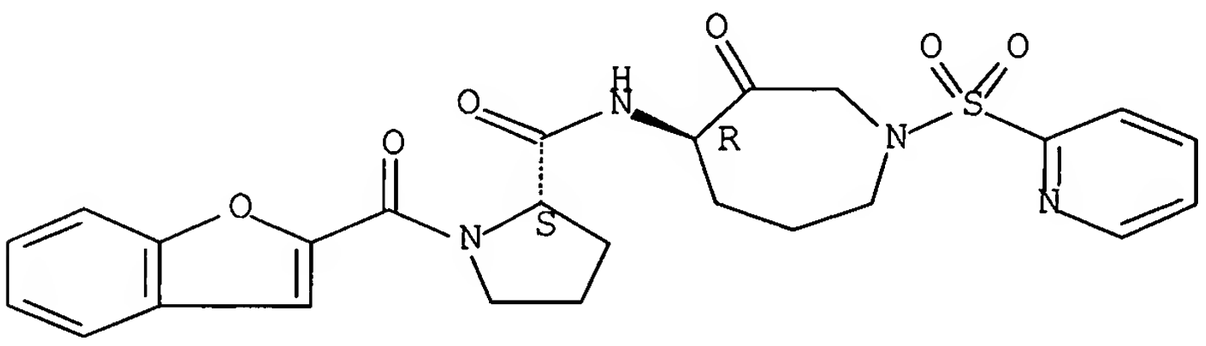
II

AB The title compds. [I; R1 = COCR13NR11R12, COCR13XR15, COCH2R13; R2 = H, alkyl, cycloalkylalkyl, etc.; R3 = H, alkyl, cycloalkylalkyl, etc.; R4 = H, alkyl, arylalkyl, etc.; R11 = H, alkyl, arylalkyl, etc.; R12 = H, alkyl, cycloalkyl, etc.; R13 = H, alkyl, alkenyl, etc.; R15 = H, alkyl, alkenyl, etc.] which inhibit proteases (no data), including cathepsin K, and are useful for treating diseases of excessive bone loss or cartilage or matrix degradation including osteoporosis, gingival disease including gingivitis and periodontitis, arthritis, more specifically, osteoarthritis and rheumatoid arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease, were prepared E.g., a multi-step synthesis of compound II was given. Compds. I are effective at 0.4-400 mg/kg/day.

IT 281216-56-6P 281218-62-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-amino-azepan-3-one protease inhibitors)

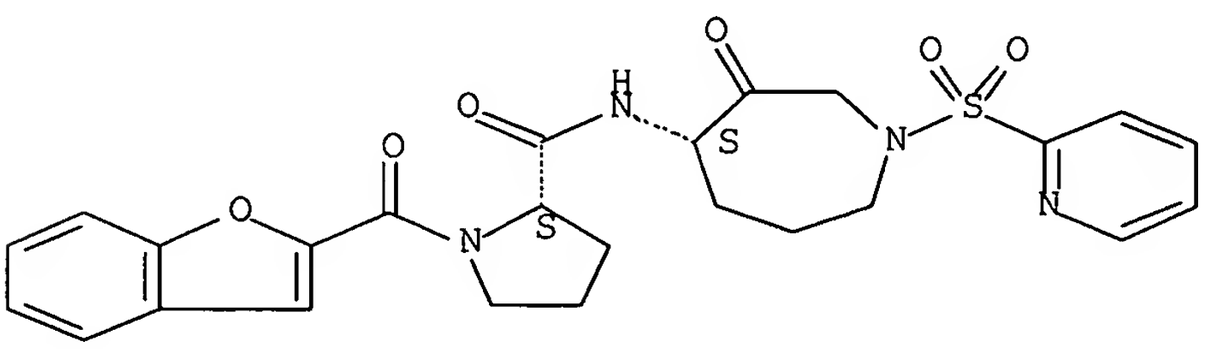
RN 281216-56-6 CAPLUS
CN 2-Pyrrolidinecarboxamide, 1-(2-benzofuranylcarbonyl)-N-[(4R)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



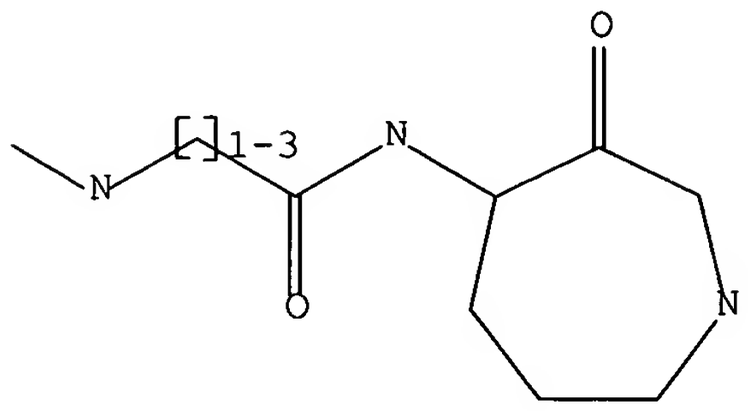
RN 281218-62-0 CAPLUS
CN 2-Pyrrolidinecarboxamide, 1-(2-benzofuranylcarbonyl)-N-[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



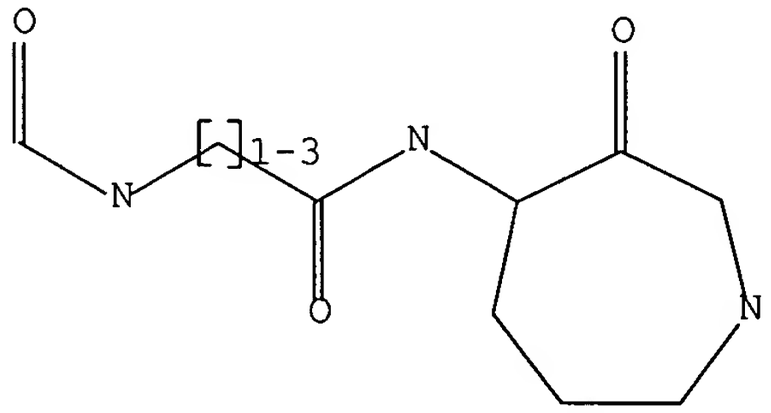
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l1; d l4; d his; log y
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

L4 HAS NO ANSWERS
L4 STR



Structure attributes must be viewed using STN Express query preparation.

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FILE 'REGISTRY' ENTERED AT 21:24:01 ON 26 JUL 2006
L1 STRUCTURE UPLOADED
L2 2 S L1
L3 32 S L1 FUL

FILE 'REGISTRY' ENTERED AT 21:24:25 ON 26 JUL 2006
L4 STRUCTURE UPLOADED
L5 2 S L4 SAM SUB=L3
L6 32 S L4 FUL SUB=L3

FILE 'CAPLUS' ENTERED AT 21:25:52 ON 26 JUL 2006
L7 4 S L6

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	20.90	228.33

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.00	-3.00

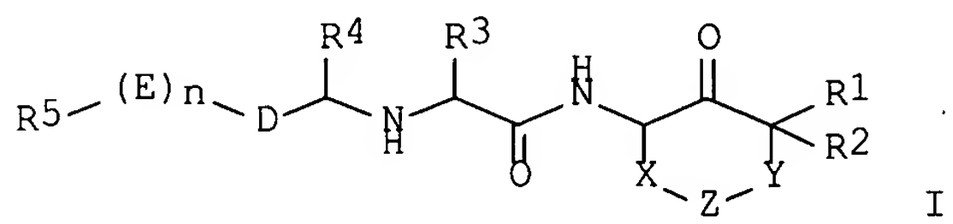
STN INTERNATIONAL LOGOFF AT 21:26:41 ON 26 JUL 2006

L8 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:638869 CAPLUS Full-text
DN 143:133700
TI Preparation of peptides as cathepsin cysteine protease inhibitors
IN Bayly, Christopher; Black, Cameron; Therien, Michel
PA Merck Frosst Canada & Co., Can.
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005066159	A1	20050721	WO 2005-CA7	20050106

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2004-534920P P 20040108
OS MARPAT 143:133700
GI



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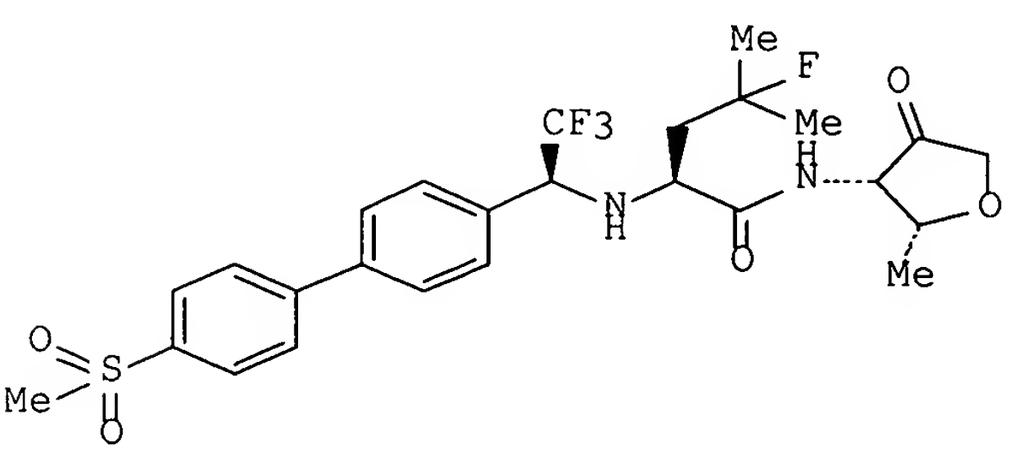

II

AB The invention relates to novel leucinamide derivs. I [X is (CR1R2)0-2; Y, Z are independently CR1R2, O, S, SO2, CO, NH or substituted imino; D, E are independently (un)substituted aryl or heteroaryl; n is 0 or 1; R1, R2 are independently H, halo or (un)substituted alkyl; or CR1R2 is a ring; R3 is alkyl or alkenyl; R4 is haloalkyl; R5 is H, alkyl, alkoxy, aryl, heteroaryl, cycloalkyl, heterocyclyl, OH, acyl, etc.] or their pharmaceutically-acceptable salts or stereoisomers, which are cathepsin cysteine protease inhibitors useful for treating and preventing cathepsin dependent conditions, e.g., osteoporosis, in which inhibition of bone resorption is indicated. Thus, peptide II was prepared by coupling of N-[(1S)-1-(4-bromophenyl)-2,2,2-trifluoroethyl]-4-fluoro-L-leucine with (4S,5R)-4-amino-5-methyldihydrofuran-3(2H)-one and [4- (methylthio)phenyl]boronic acid, followed by S-oxidation

IT 858945-73-0P 858945-74-1P 858945-75-2P
858945-76-3P 858945-80-9P 858945-81-0P
858945-82-1P 858945-83-2P 858945-84-3P

858945-85-4P 858945-86-5P 858945-87-6P
858945-88-7P 858945-89-8P 858945-90-1P
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858945-94-5P 858945-95-6P 858945-96-7P
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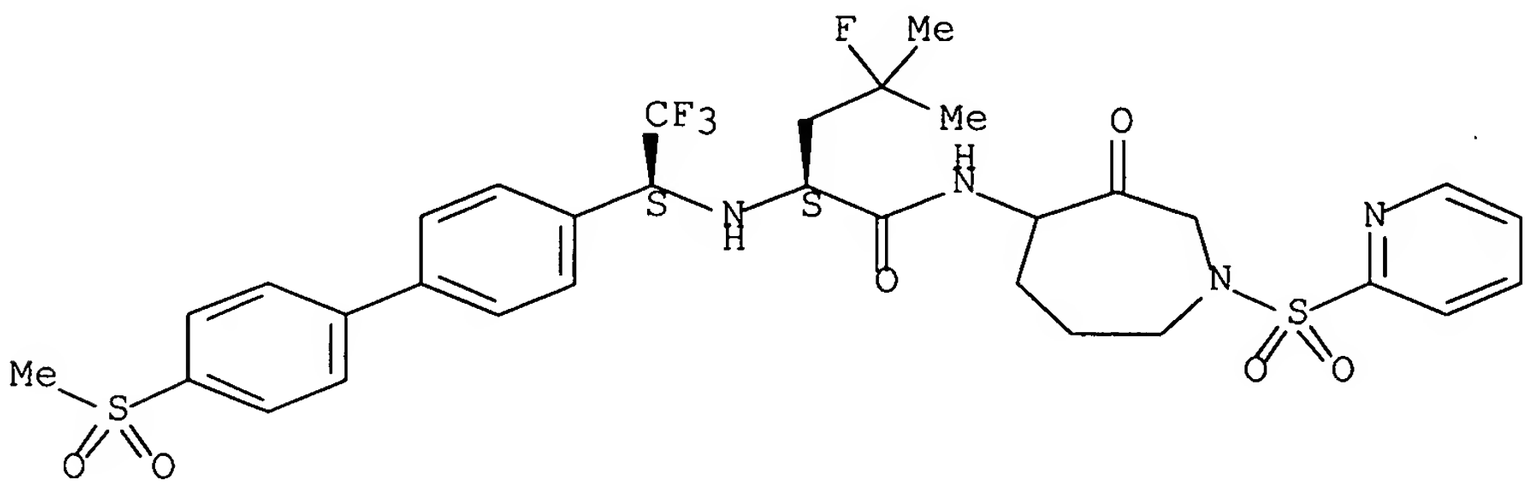
858946-06-2P 858946-08-4P 858946-10-8P
858946-12-0P 858946-14-2P 858946-16-4P
858946-36-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides as cathepsin cysteine protease inhibitors)

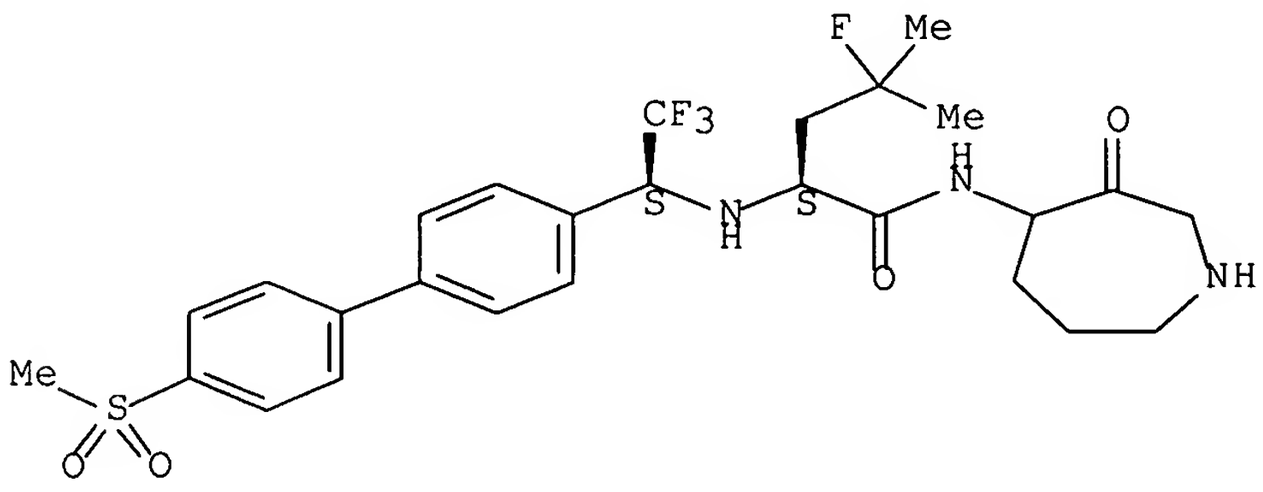
RN 858945-73-0 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



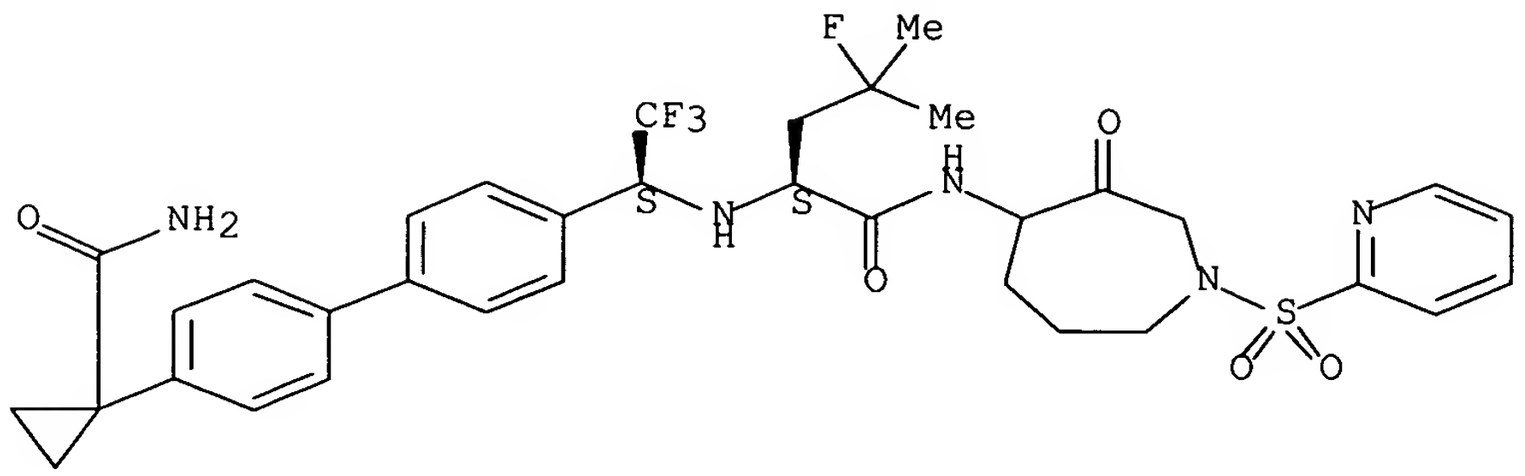
RN 858945-74-1 CAPLUS
CN Pentanamide, 4-fluoro-N-(hexahydro-3-oxo-1H-azepin-4-yl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



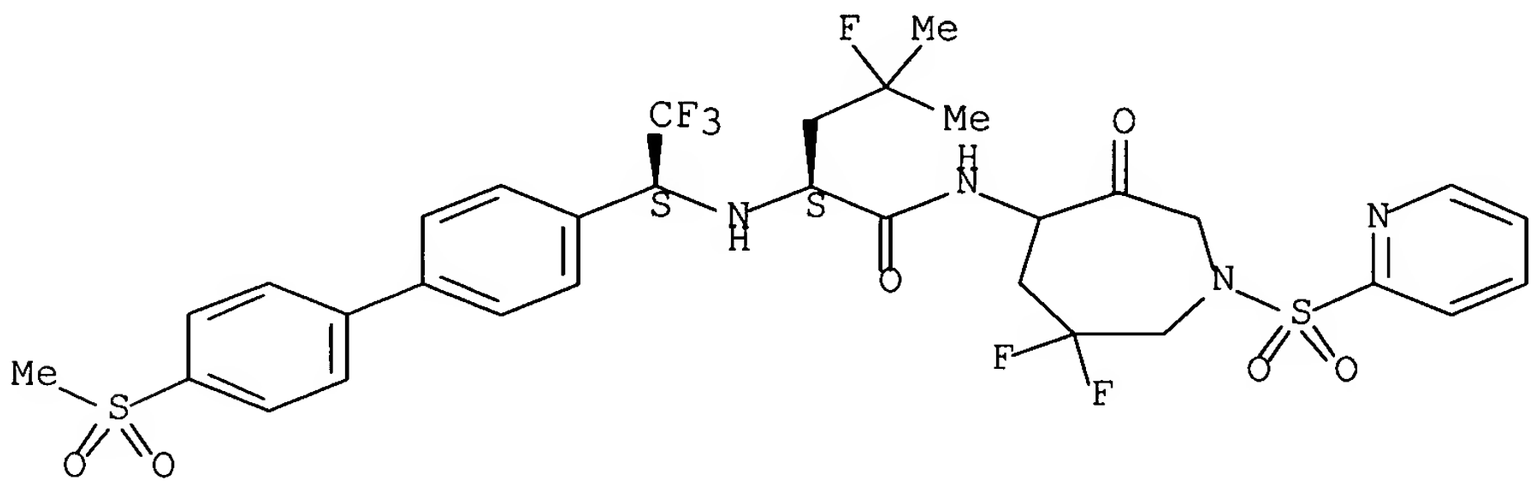
RN 858945-75-2 CAPLUS
CN Cyclopropanecarboxamide, 1-[4'-[(1S)-2,2,2-trifluoro-1-[[(1S)-3-fluoro-1-[[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]amino]ethyl][1,1'-biphenyl]-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



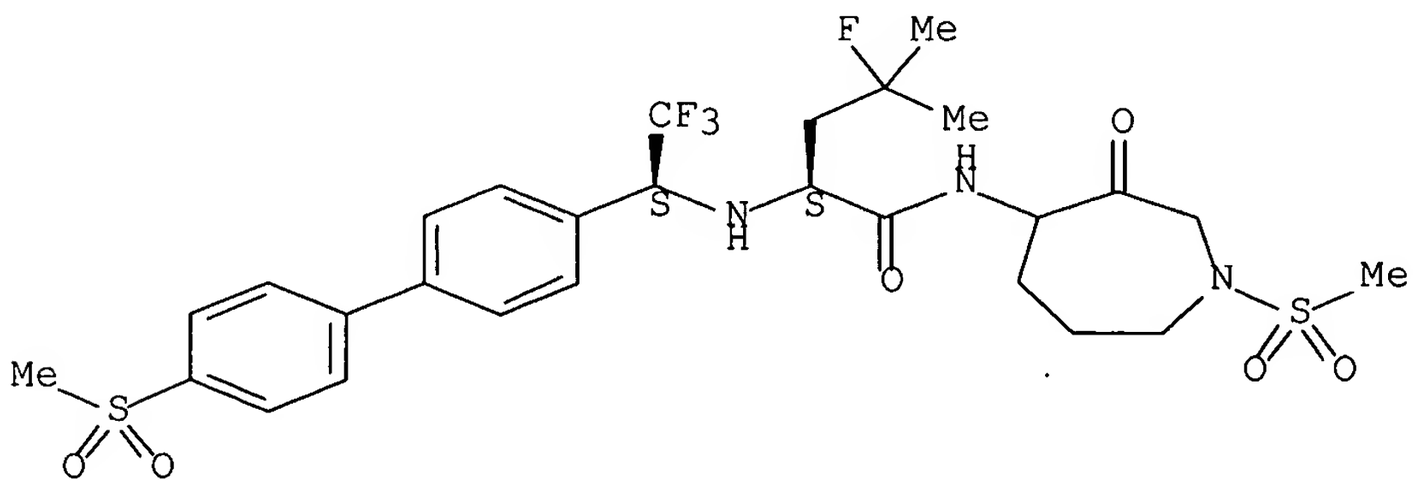
RN 858945-76-3 CAPLUS
CN Pentanamide, N-[6,6-difluorohexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-fluoro-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



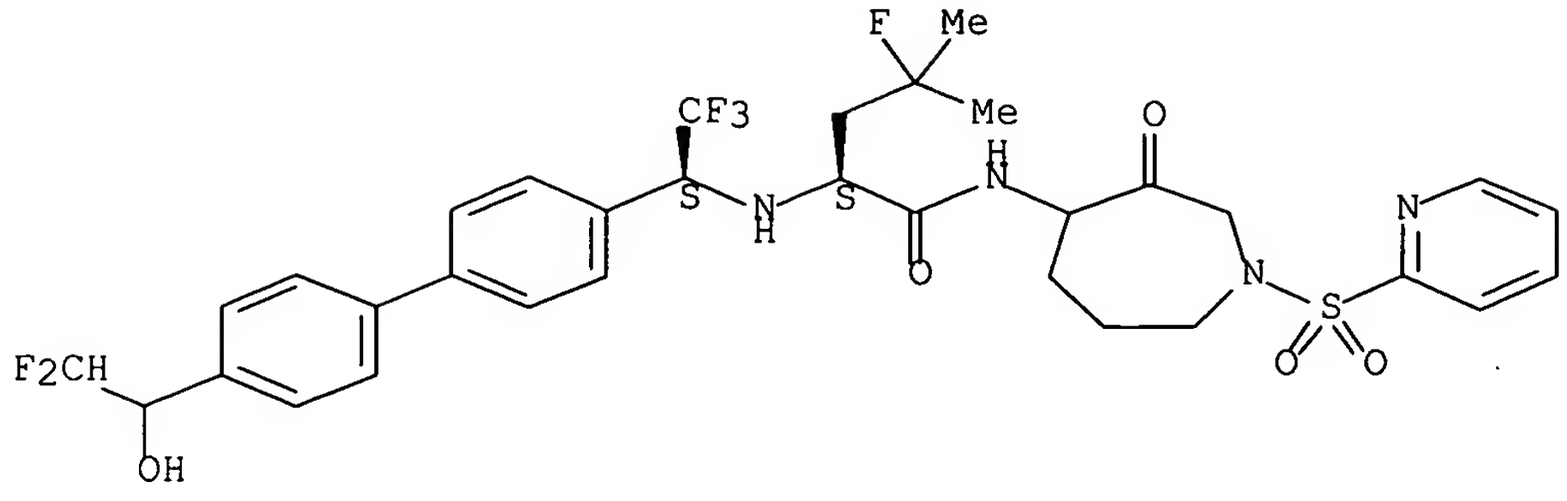
RN 858945-80-9 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-1-(methylsulfonyl)-3-oxo-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



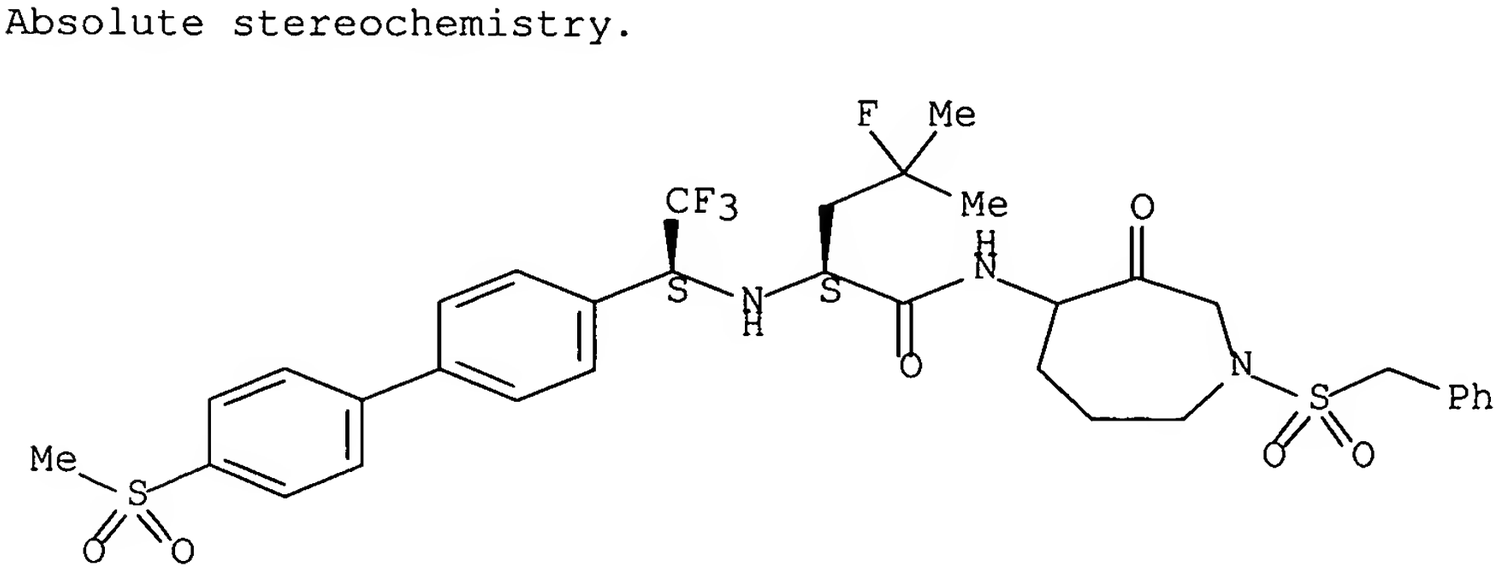
RN 858945-81-0 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4'-(2,2-difluoro-1-hydroxyethyl)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



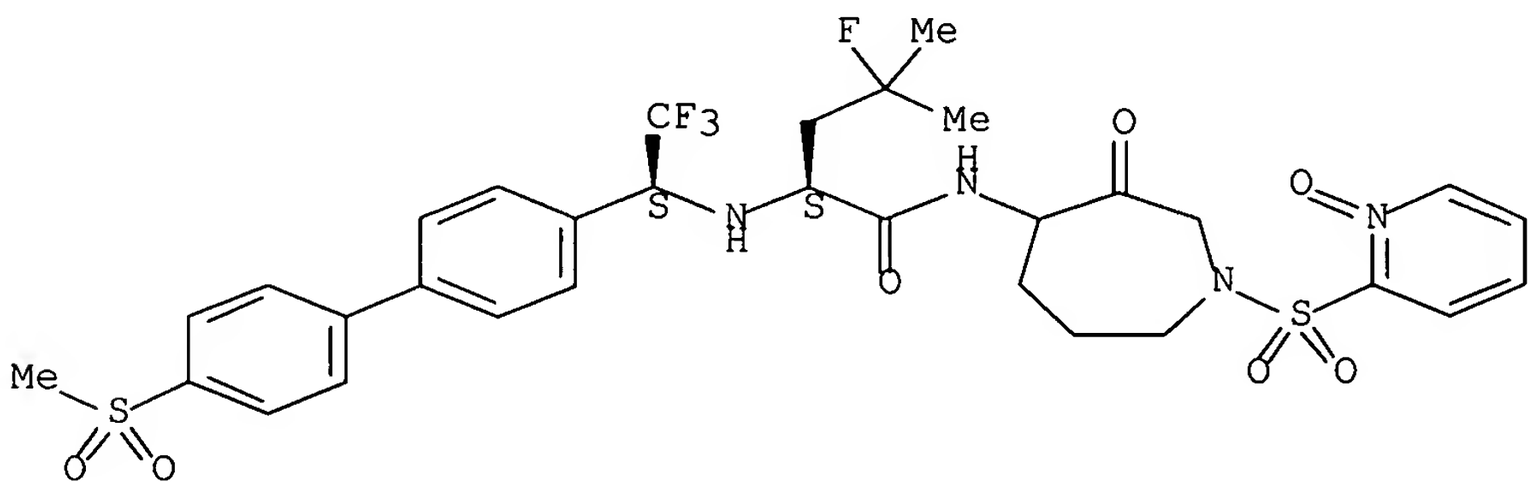
RN 858945-82-1 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-[(phenylmethyl)sulfonyl]-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



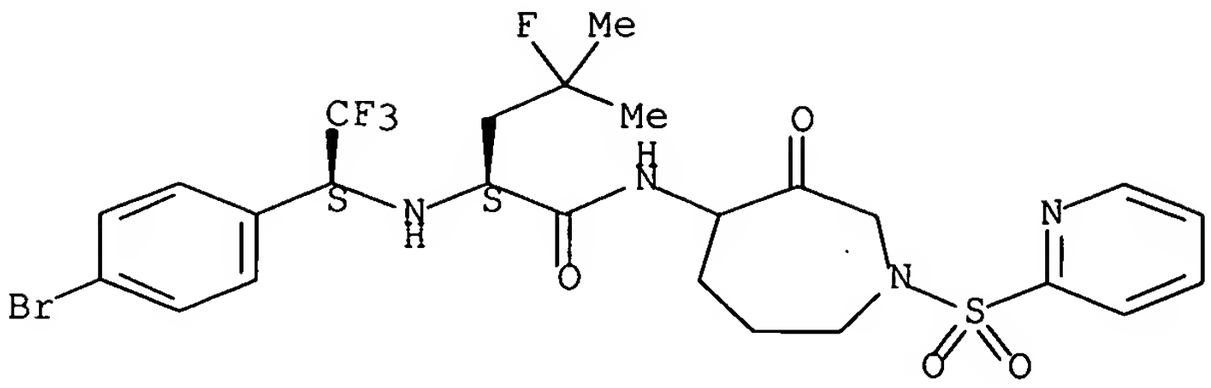
RN 858945-83-2 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-1-[(1-oxido-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



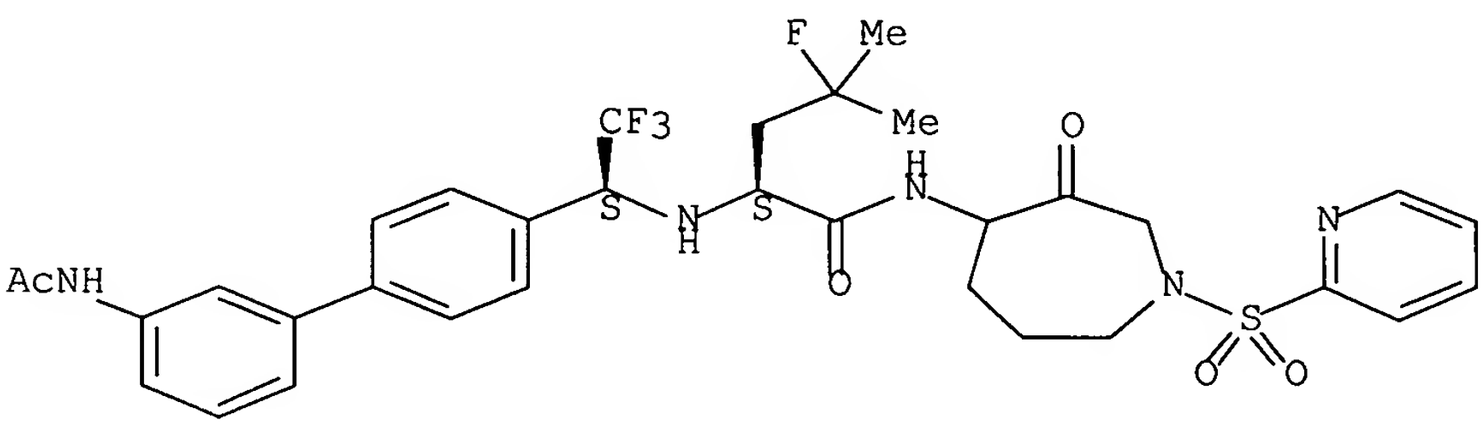
RN 858945-84-3 CAPLUS
CN Pentanamide, 2-[[(1S)-1-(4-bromophenyl)-2,2,2-trifluoroethyl]amino]-4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



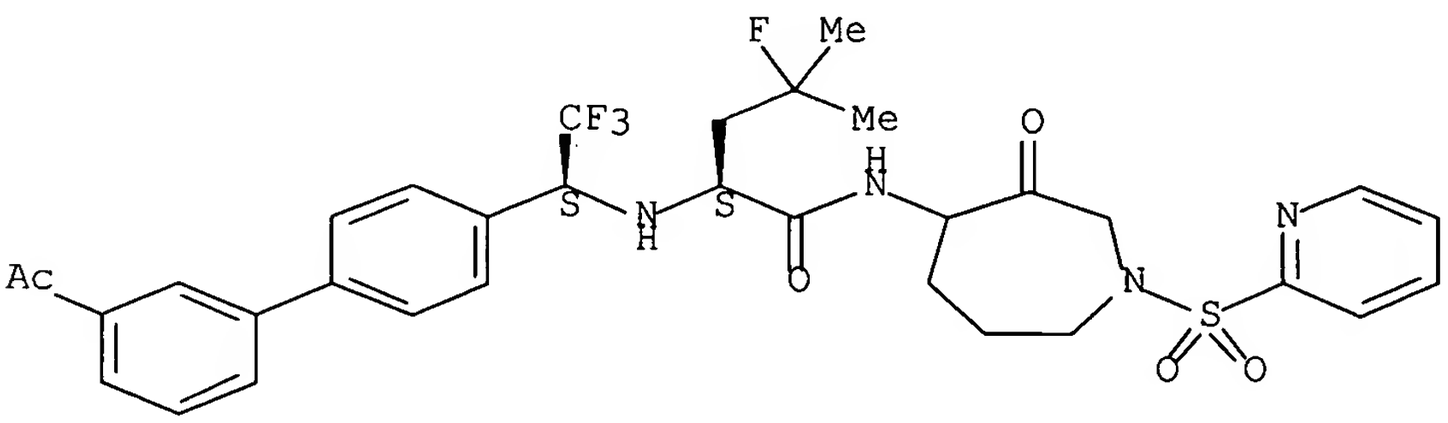
RN 858945-85-4 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[3'-(acetylamino)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



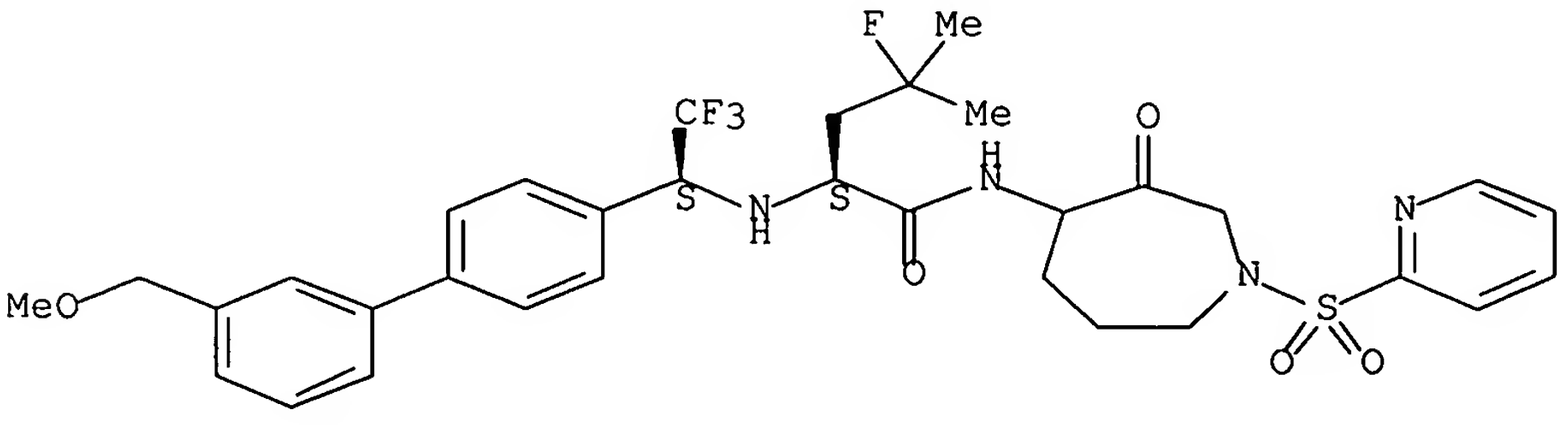
RN 858945-86-5 CAPLUS
CN Pentanamide, 2-[[(1S)-1-(3'-acetyl[1,1'-biphenyl]-4-yl)-2,2,2-trifluoroethyl]amino]-4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 858945-87-6 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[3'-(methoxymethyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

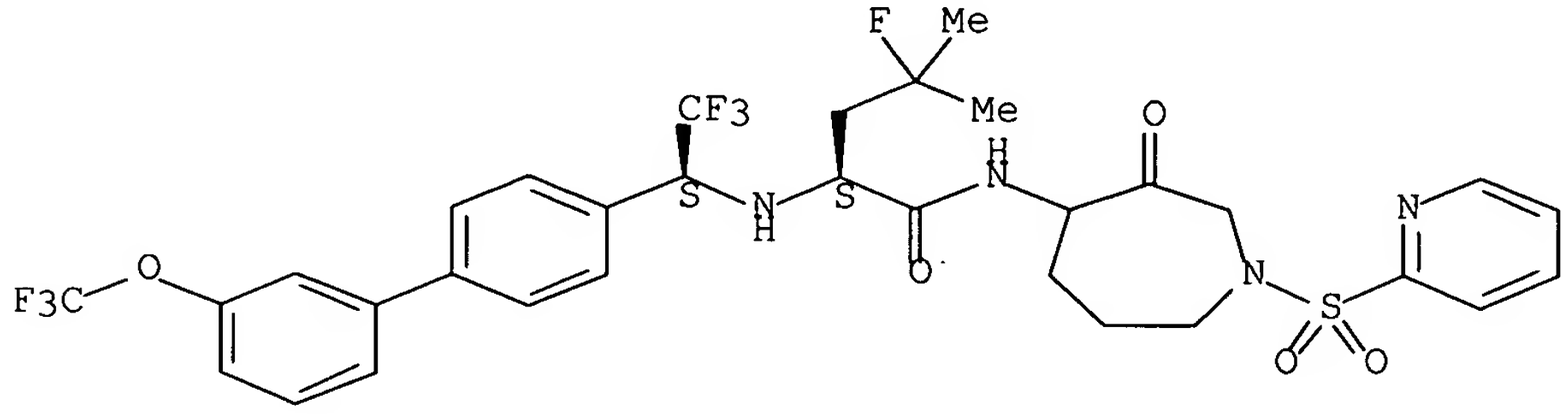
Absolute stereochemistry.



RN 858945-88-7 CAPLUS

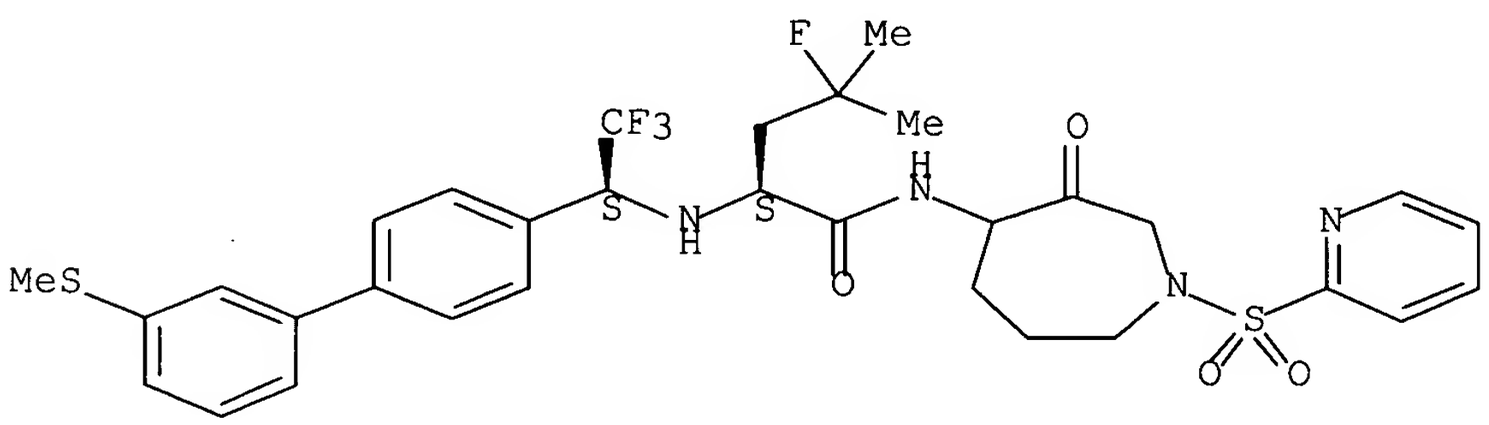
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



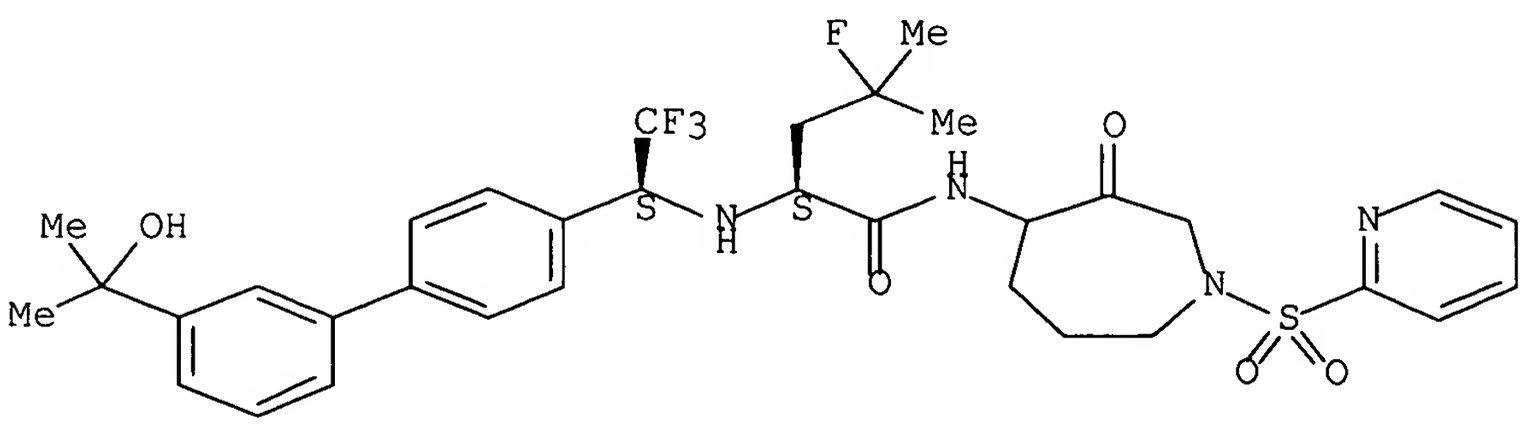
RN 858945-89-8 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[3'-(methylthio)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



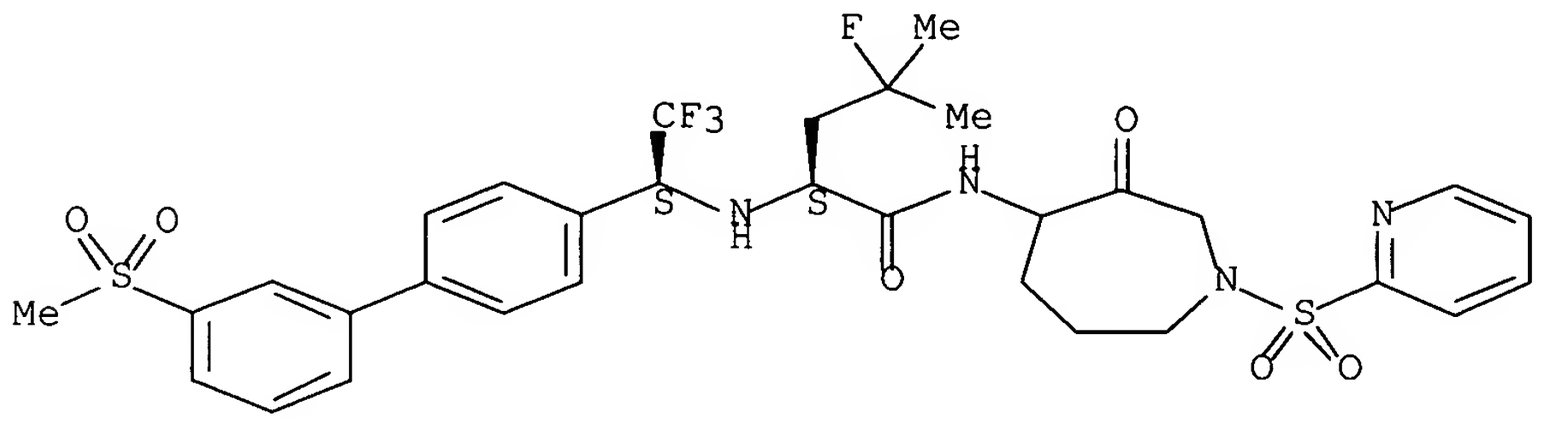
RN 858945-90-1 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[3'-(1-hydroxy-1-methylethyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



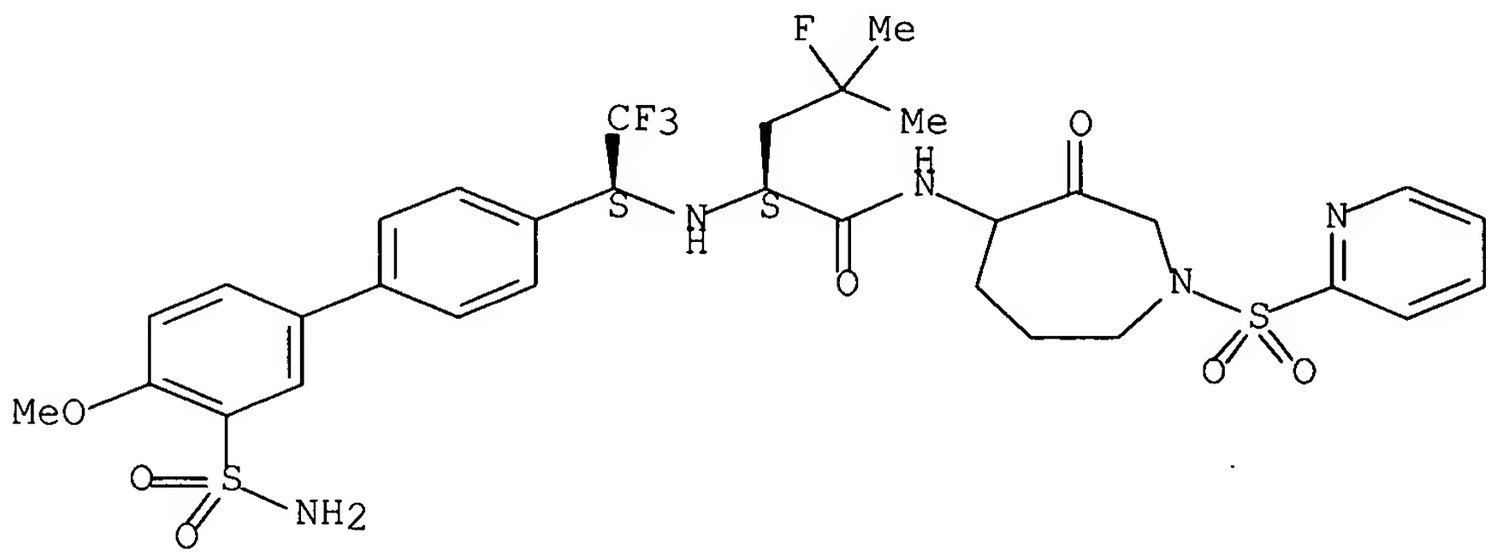
RN 858945-91-2 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[3'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 858945-92-3 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[3'-(aminosulfonyl)-4'-methoxy[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

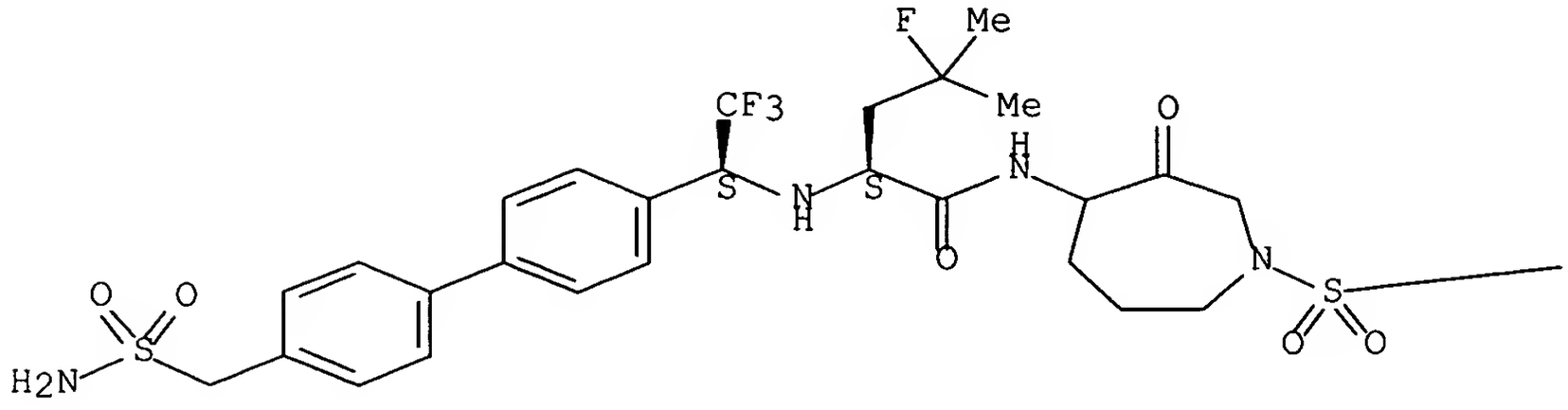
Absolute stereochemistry.



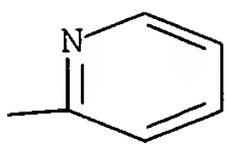
RN 858945-93-4 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4'-[(aminosulfonyl)methyl][1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



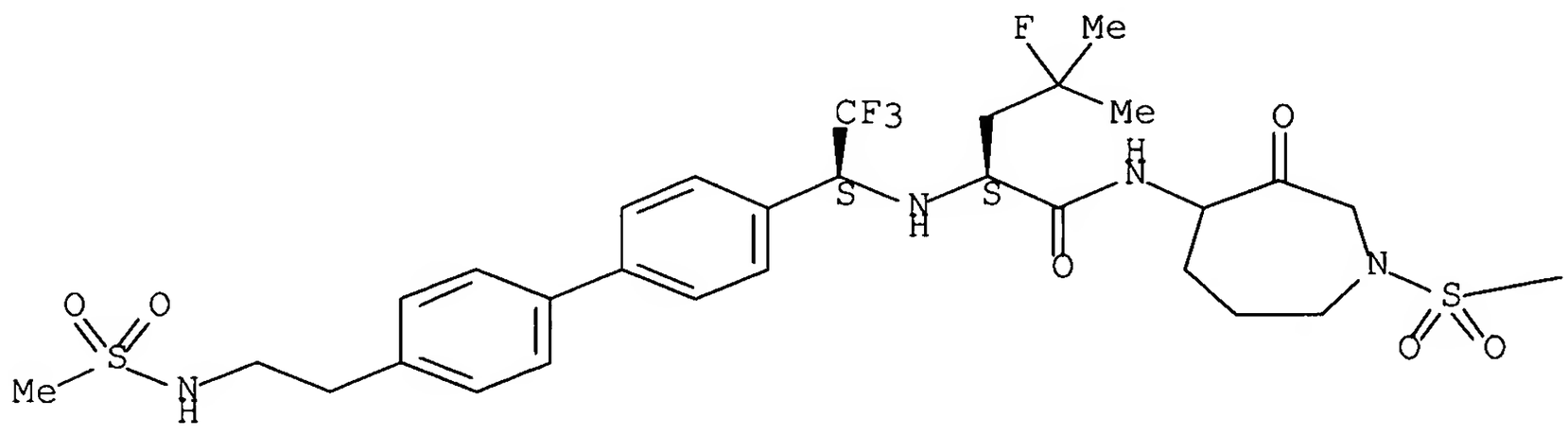
PAGE 1-B



RN 858945-94-5 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-[2-[(methylsulfonyl)amino]ethyl][1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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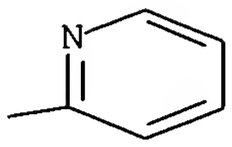
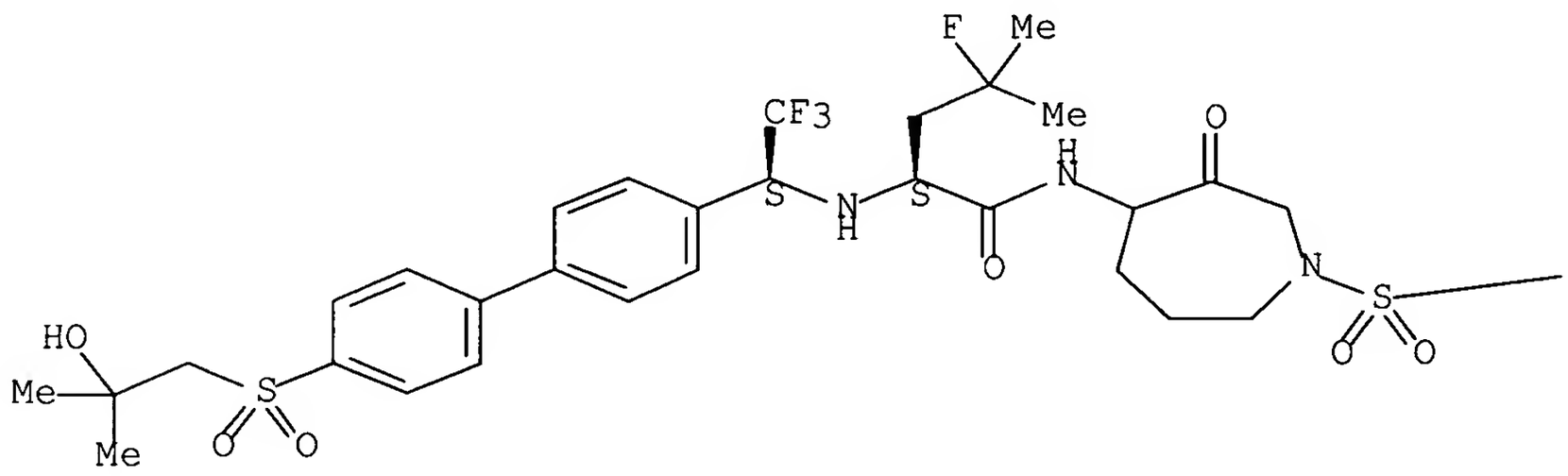


RN 858945-95-6 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-[(2-hydroxy-2-methylpropyl)sulfonyl][1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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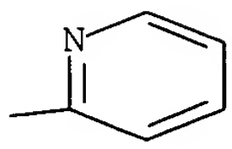
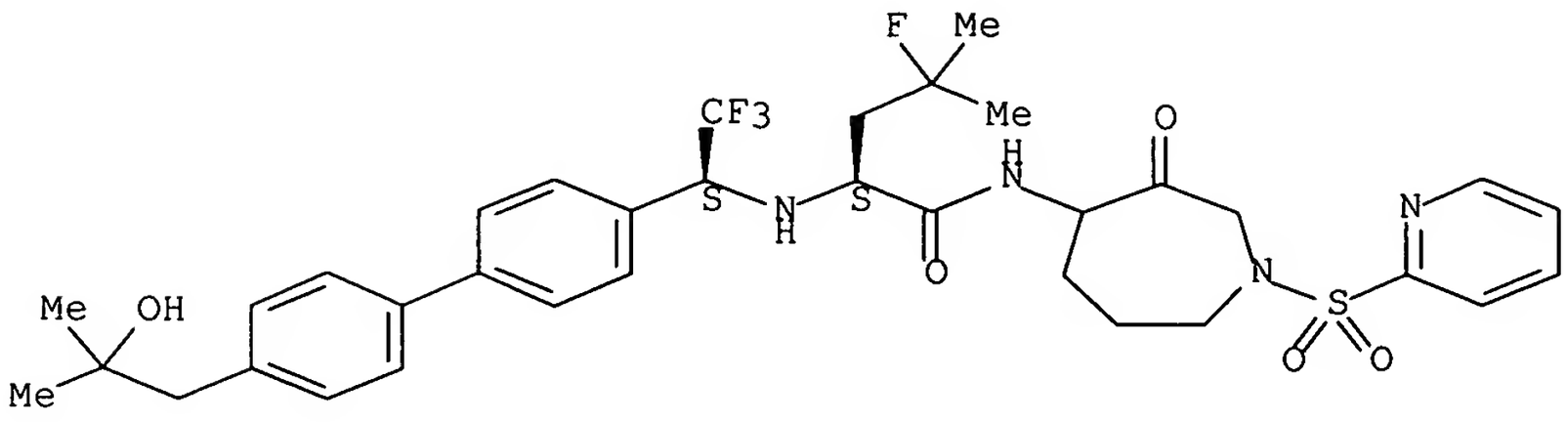


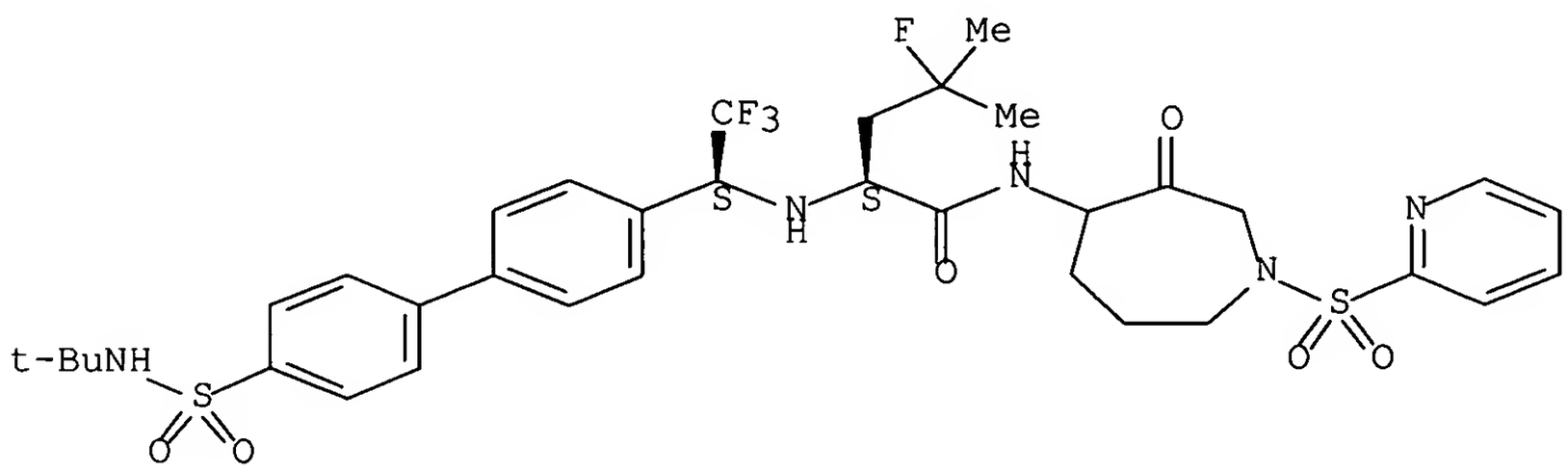
RN 858945-96-7 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(2-hydroxy-2-methylpropyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



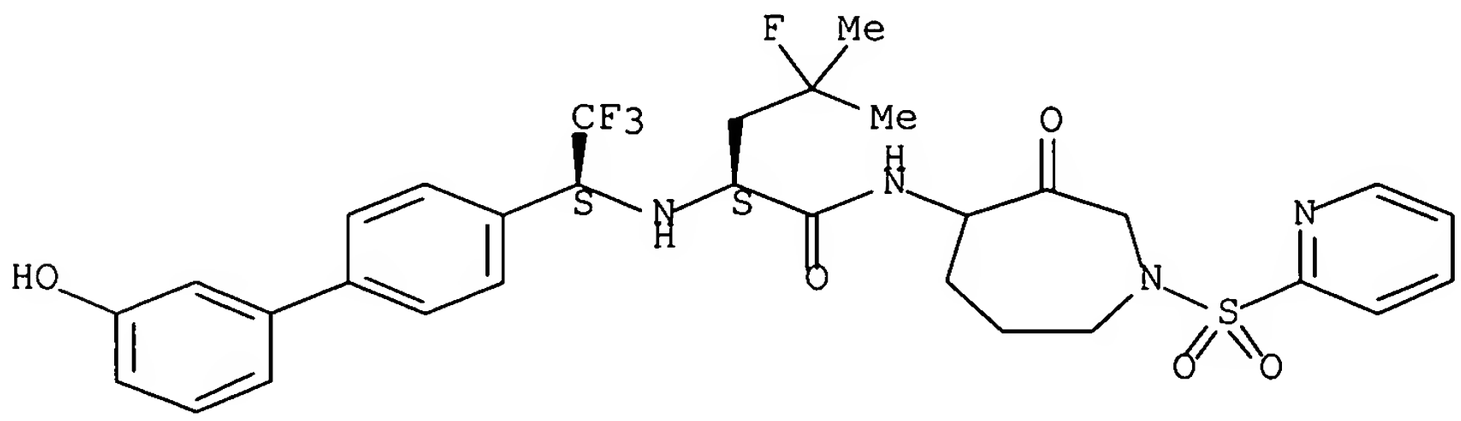
RN 858945-97-8 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4'-[[(1,1-dimethylethyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 858945-98-9 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(3'-hydroxy[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

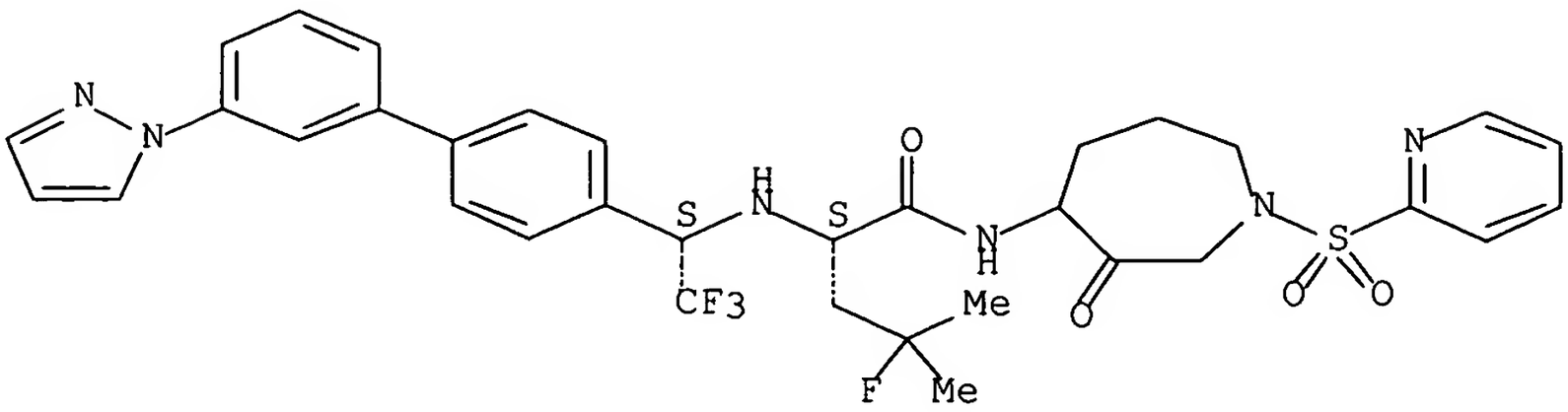
Absolute stereochemistry.



RN 858945-99-0 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[3'-(1H-pyrazol-1-yl)[1,1'-

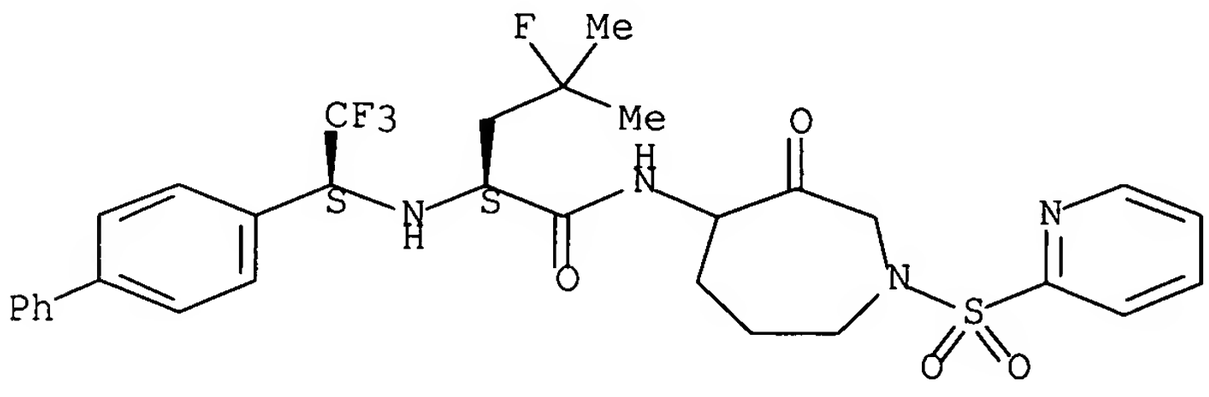
biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



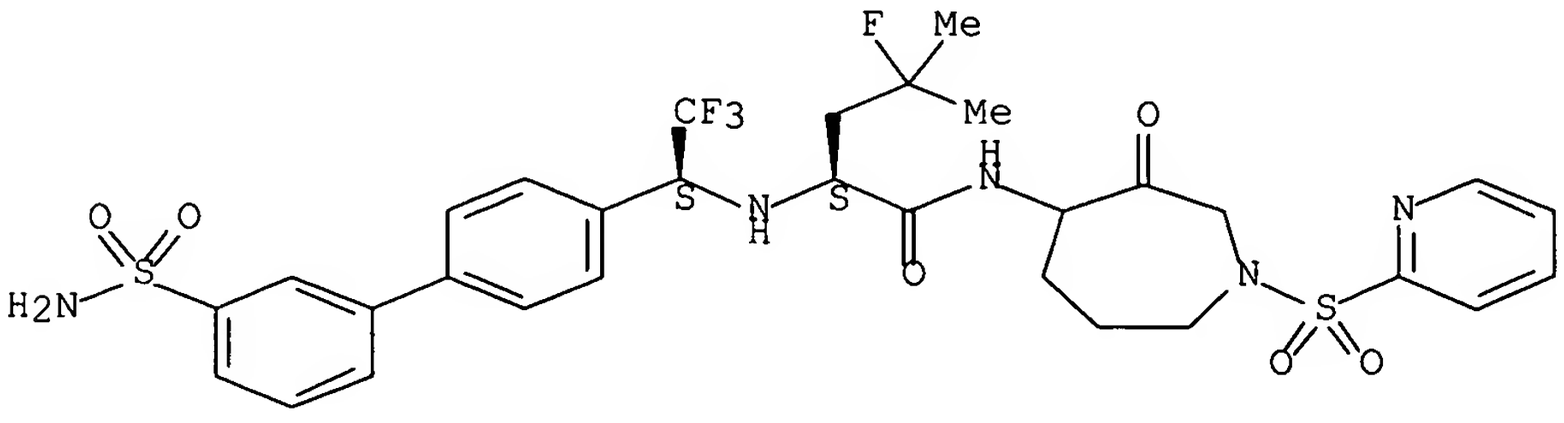
RN 858946-00-6 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[1,1'-biphenyl]-4-yl-2,2,2-trifluoroethyl]amino]-4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 858946-02-8 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[3'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

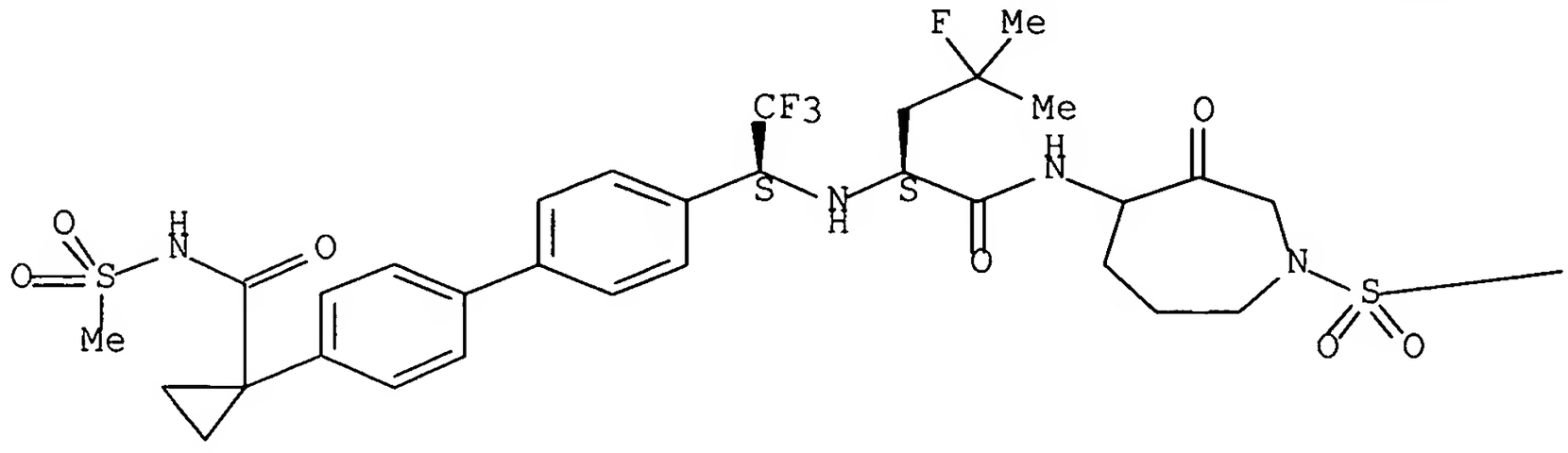


RN 858946-04-0 CAPLUS
CN Cyclopropanecarboxamide, N-(methylsulfonyl)-1-[4'-[(1S)-2,2,2-trifluoro-1-

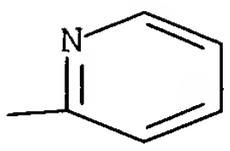
[[(1S)-3-fluoro-1-[[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]amino]ethyl][1,1'-biphenyl]-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

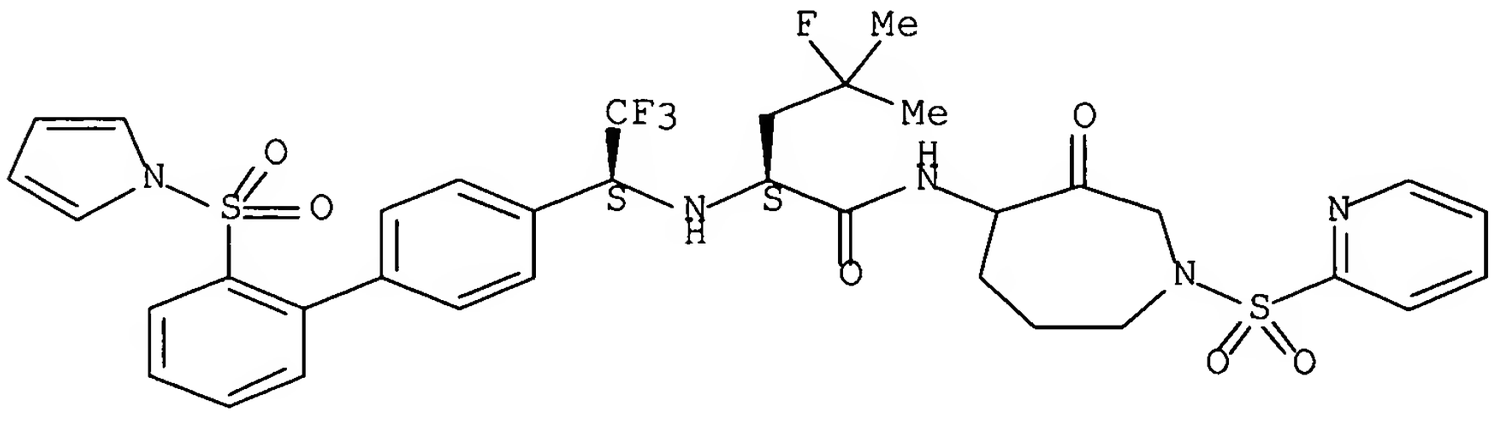


PAGE 1-B



RN 858946-06-2 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[2'-(1H-pyrrol-1-ylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

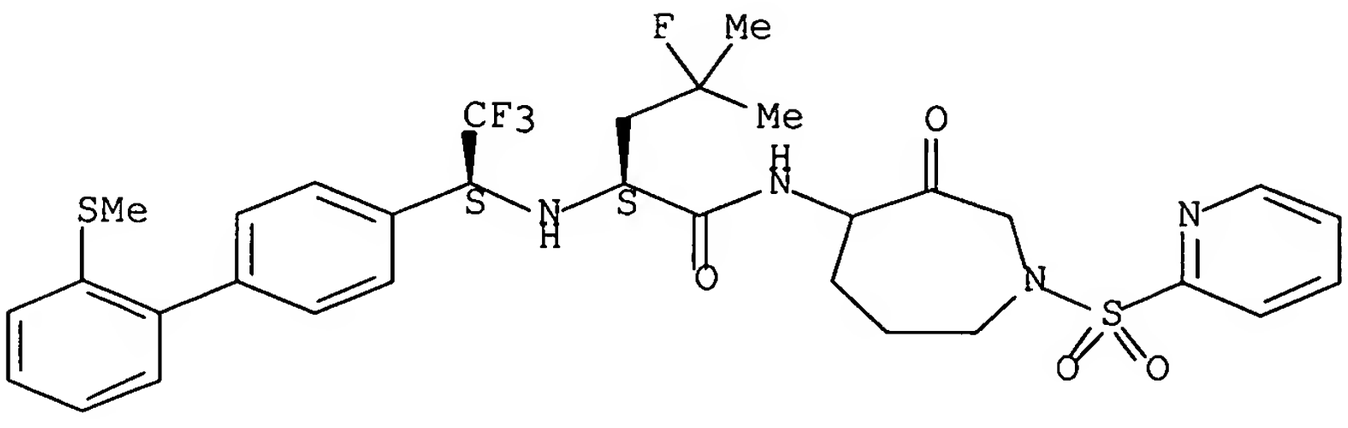
Absolute stereochemistry.



RN 858946-08-4 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-

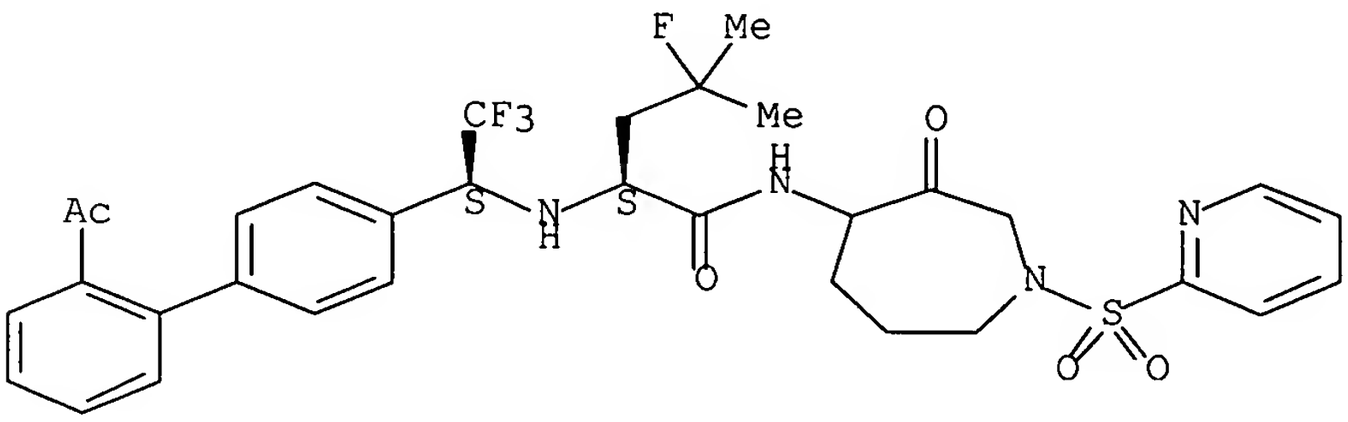
4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[2'-(methylthio)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



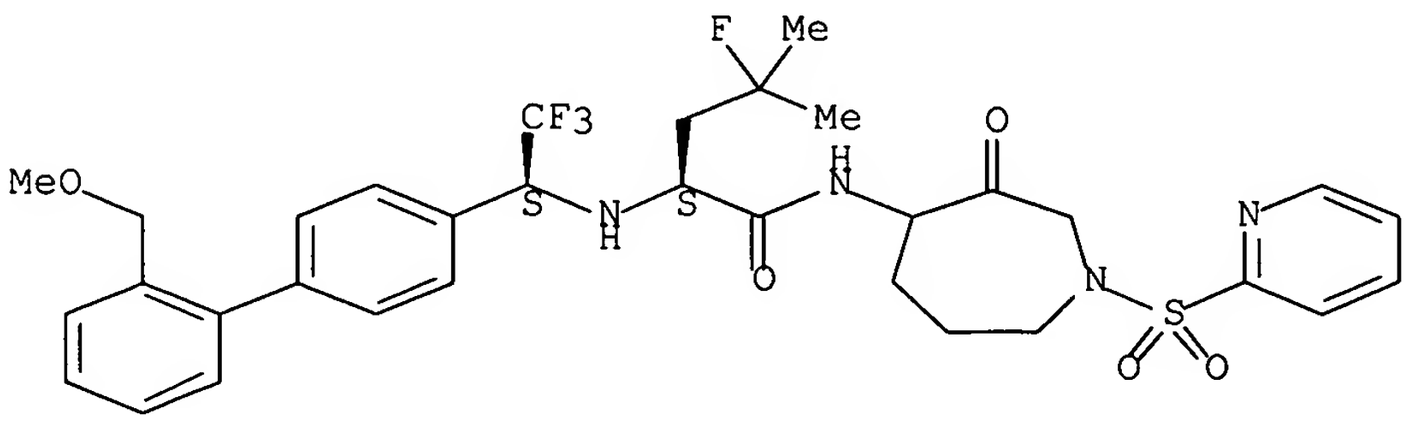
RN 858946-10-8 CAPLUS
CN Pentanamide, 2-[[(1S)-1-(2'-acetyl[1,1'-biphenyl]-4-yl)-2,2,2-trifluoroethyl]amino]-4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



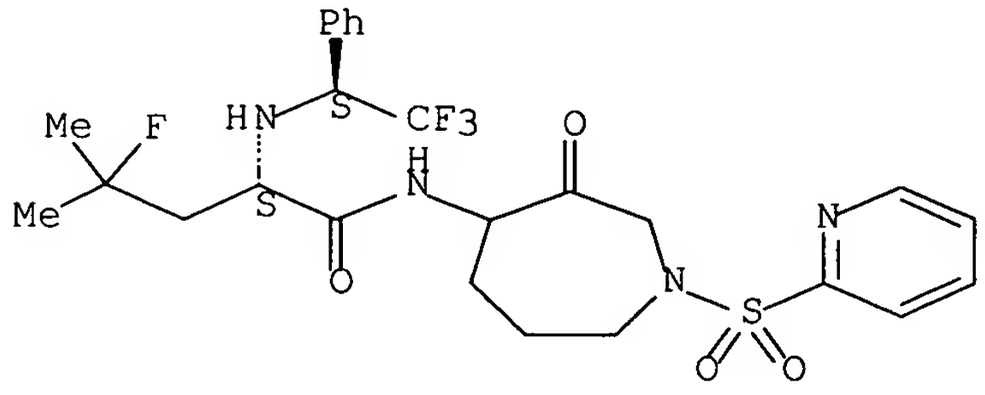
RN 858946-12-0 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[2'-(methoxymethyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



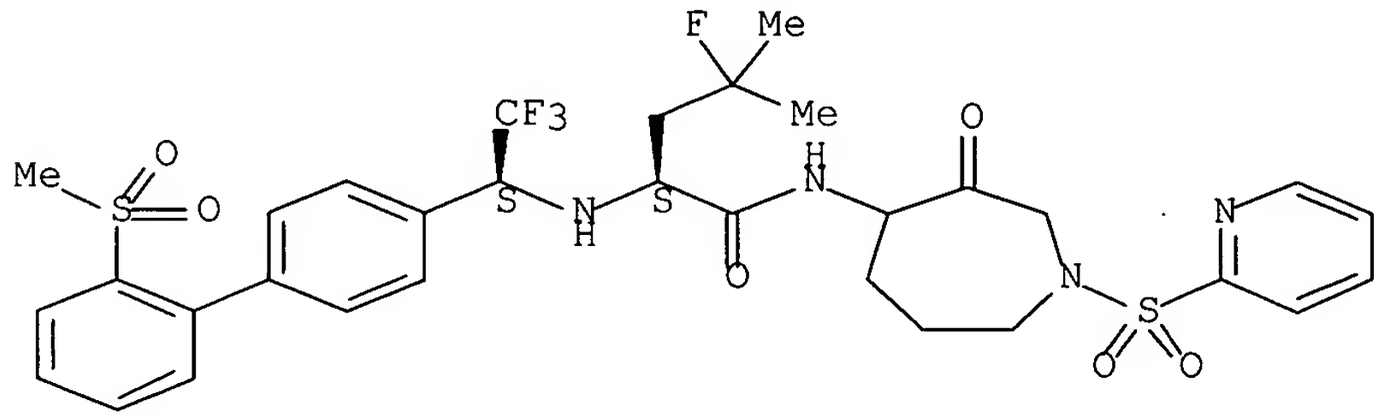
RN 858946-14-2 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-phenylethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



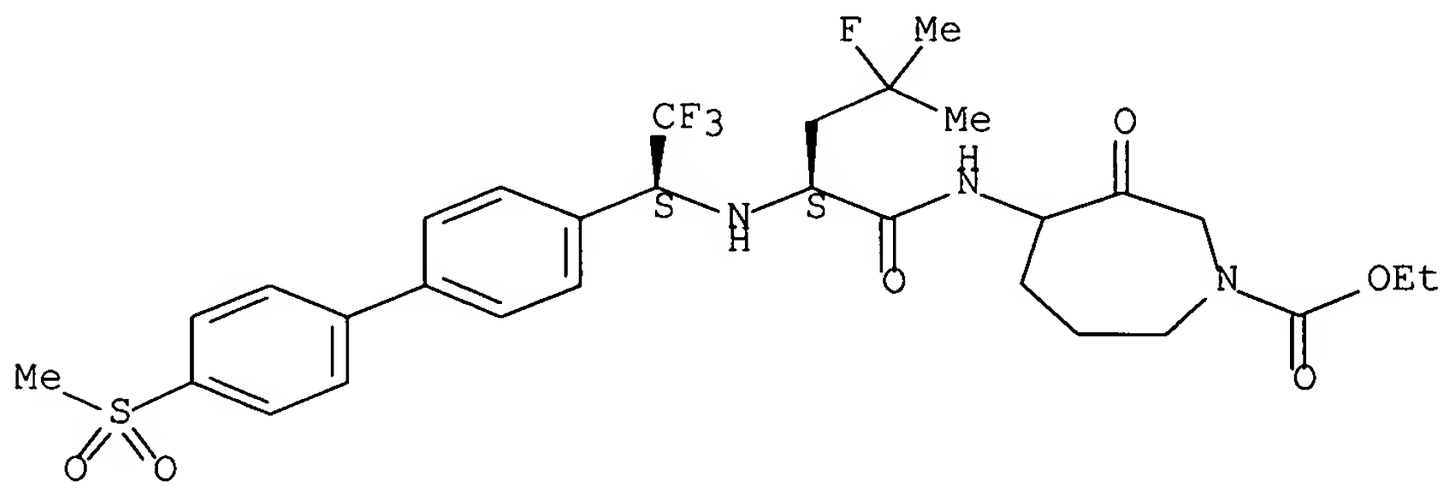
RN 858946-16-4 CAPLUS
CN Pentanamide, 4-fluoro-N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[2'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 858946-36-8 CAPLUS
CN 1H-Azepine-1-carboxylic acid, 4-[[(2S)-4-fluoro-4-methyl-1-oxo-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]pentyl]amino]hexahydro-3-oxo-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



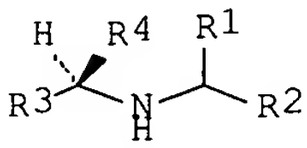
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:219775 CAPLUS Full-text
DN 142:280425
TI Preparation of amino acid derivatives as cathepsin inhibitors
IN Bayly, Christopher; Black, Cameron; McKay, Daniel J.
PA Merck Frosst Canada & Co., Can.
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005021487	A1	20050310	WO 2004-CA1577	20040823
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004268707	A1	20050310	AU 2004-268707	20040823
	CA 2535366	AA	20050310	CA 2004-2535366	20040823
	EP 1660436	A1	20060531	EP 2004-761741	20040823
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
PRAI	US 2003-498017P	P	20030827		
	WO 2004-CA1577	W	20040823		

60/498,017 → no Cont. data

OS MARPAT 142:280425
GI



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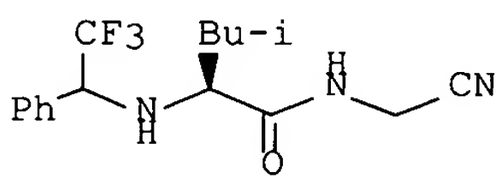


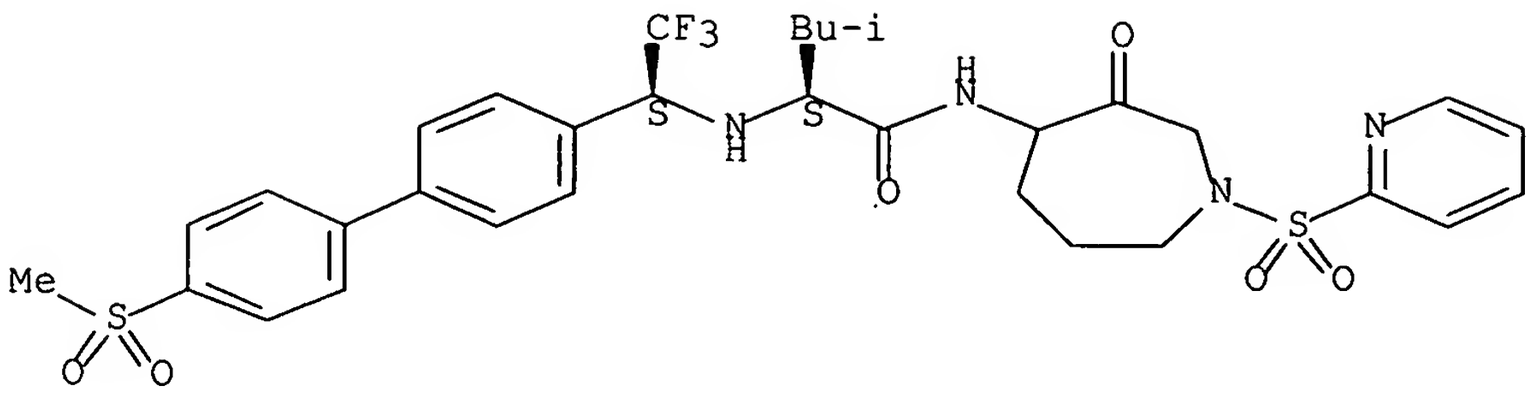
II

AB The invention relates to compds. I which are cysteine protease inhibitors, including but not limited to inhibitors of cathepsins K, L, S and B, and are useful for treating diseases in which inhibition of bone resorption is indicated, e.g., osteoporosis, osteoarthritis and rheumatoid arthritis. Thus, a mixture of L-leucine Me ester hydrochloride, 2,2,2- trifluoroacetophenone, diisopropylethylamine and TiCl4 in CH2Cl2 was stirred overnight, addnl. TiCl4 added, and the mixture stirred an addnl. 3 h. A solution of NaCNBH3 in MeOH was added and the mixture stirred 2 h to afford Me N-(2,2,2-trifluoro-1-phenylethyl)-L-leucinate. Saponification of the ester and reaction with aminoacetonitrile hydrochloride in DMF in the presence of PyBOP and Et3N yielded L-leucinamide derivative II.

IT 678982-29-1P 847361-59-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid derivs. as cathepsin inhibitors)

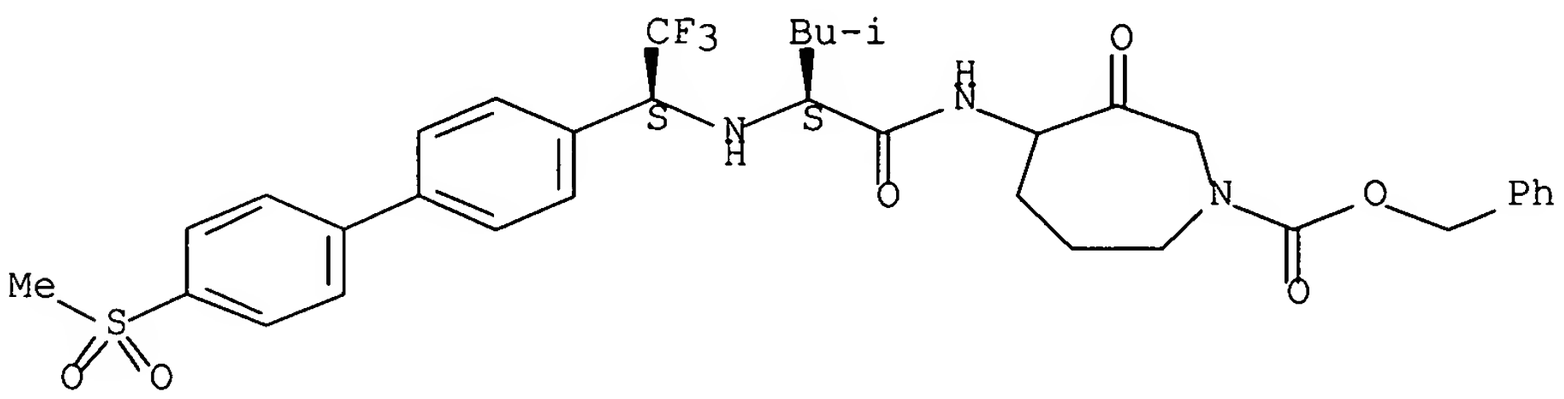
RN 678982-29-1 CAPLUS
CN Pentanamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 847361-59-5 CAPLUS
CN 1H-Azepine-1-carboxylic acid, hexahydro-4-[[(2S)-4-methyl-1-oxo-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]pentyl]amino]-3-oxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:333709 CAPLUS Full-text

DN 140:321727

TI Preparation of 4-aminoazepan-3-one peptides as cathepsin K inhibitors useful in the treatment of osteoporosis

IN Black, Cameron

PA Merck Frosst Canada & Co., Can.

SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004033445	A1	20040422	WO 2003-CA1551	20031007
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2500317	AA	20040422	CA 2003-2500317	20031007
	AU 2003273697	A1	20040504	AU 2003-273697	20031007
	EP 1551823	A1	20050713	EP 2003-757604	20031007
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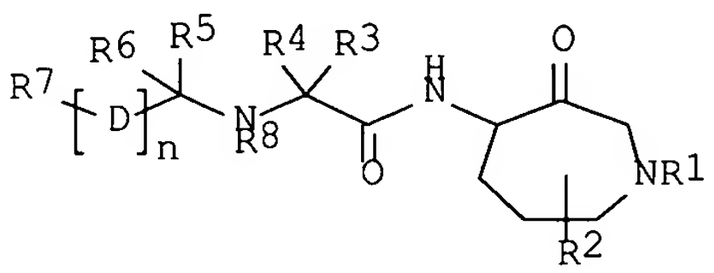
	JP 2006504719	T2	20060209	JP 2004-542127	20031007
PRAI	US 2002-416892P	P	20021008		
	WO 2003-CA1551	W	20031007		

OS MARPAT 140:321727

GI



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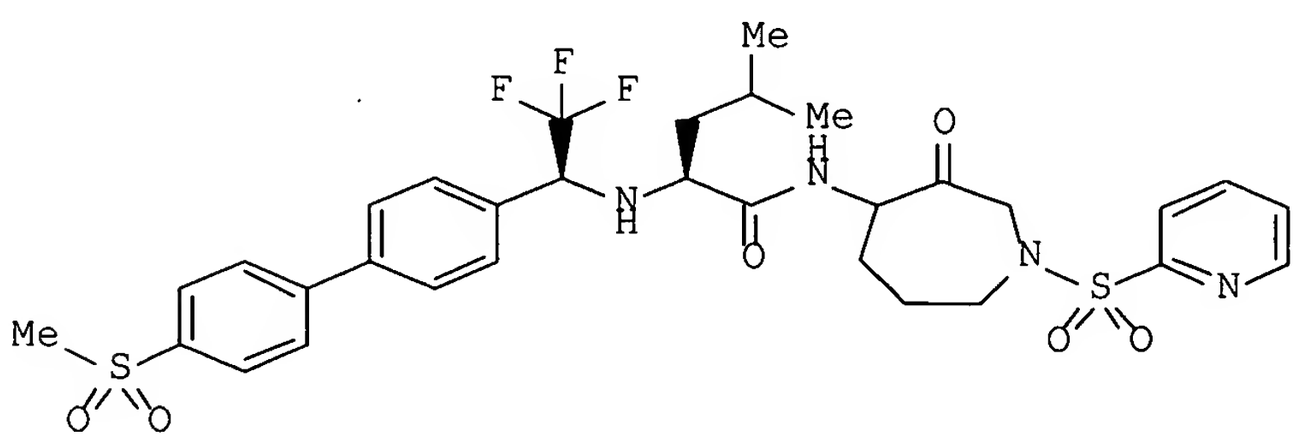


II

AB The invention relates to azepinones I [R1 is H, alkyl, a sulfonyl or acyl group, arylalkyl; R2 is H or (cyclo)alkyl; R3 is H, alk(en)yl, haloalk(en)yl or cycloalk(en)yl; or R3R4C is (un)substituted (hetero)cycloalk(en)yl; R5 is H, alkyl or haloalkyl; R6 is haloalkyl, (un)substituted (hetero)aryl or (hetero)arylalkyl; R7 is H, alk(en)(yn)yl, alkoxy, halo, nitro, cyano, (hetero)aryl, carboxy, etc.; D is (un)substituted alk(en)ylene or (hetero)arylene; n is 0-3] or their pharmaceutically-acceptable salts, stereoisomers and N-oxides which are cysteine protease inhibitors, in

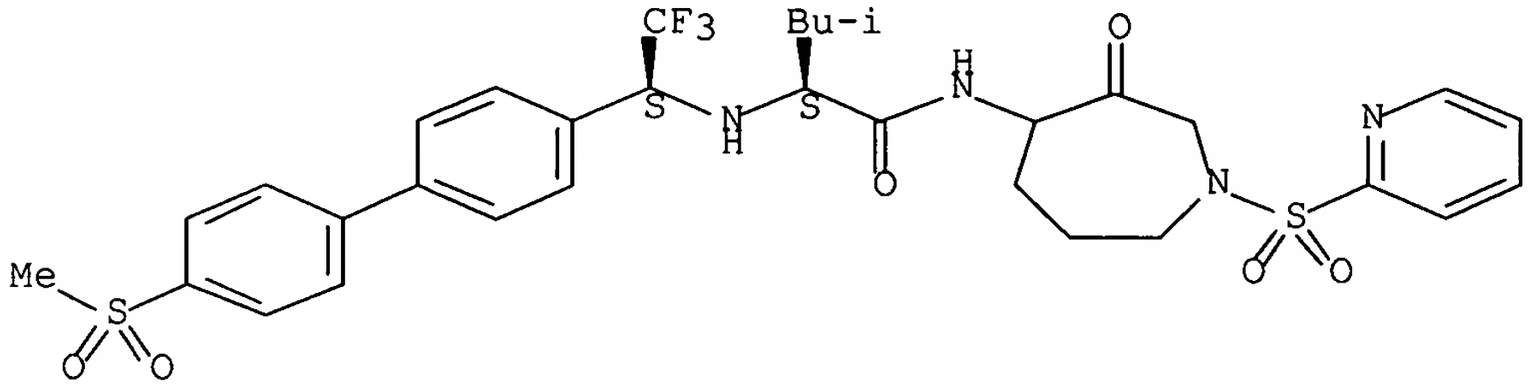
particular, inhibitors of cathepsins K, L, S and B. These compds. are useful for treating diseases, e.g., osteoporosis, in which inhibition of bone resorption is indicated. Thus, aminoazepanone peptide II was prepared by a multistep procedure starting with reaction of silyl-protected L-leucinol with trifluoroacetaldehyde Me hemiacetal.

IT 678982-29-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(preparation of aminoazepanone peptides as cathepsin K inhibitors for treatment of osteoporosis)

RN 678982-29-1 CAPLUS

CN Pentanamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:590812 CAPLUS Full-text
DN 139:133836
TI Preparation of 4-aminoazepan-3-ones as protease inhibitors
IN Marquis, Robert Wells; Ru, Yu; Veber, Daniel Frank; Cummings, Maxwell David; Thompson, Scott Kevin; Yamashita, Dennis Shinji
PA Smithkline Beecham Corporation, USA
SO U.S. Pat. Appl. Publ., 126 pp., Cont.-in-part of U.S. Ser. No. 593,845, abandoned.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003144175	A1	20030731	US 2001-881334	20010614
	WO 2000038687	A1	20000706	WO 1999-US30730	19991221
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1384713	A1	20040128	EP 2003-76211	19991221
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	ZA 2001004208	A	20020523	ZA 2001-4208	20010523
	WO 2002017924	A1	20020307	WO 2001-US27178	20010831
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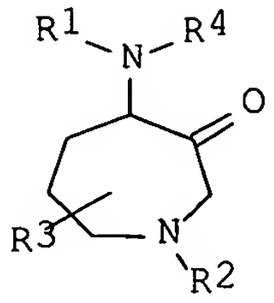
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001086983	A5	20020313	AU 2001-86983	20010831
	EP 1320370	A1	20030625	EP 2001-966474	20010831
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004509083	T2	20040325	JP 2002-522897	20010831
	US 2004002487	A1	20040101	US 2003-404716	20030401
	US 2005256104	A1	20051117	US 2005-152745	20050614
PRAI	US 1998-113636P	P	19981223		
	US 1999-164581P	P	19991110		
	WO 1999-US30730	A2	19991221		
	US 2000-593845	B2	20000614		
	EP 1999-963112	A3	19991221		
	US 2000-653815	A2	20000901		
	US 2001-881334	A2	20010614		
	WO 2001-US27178	W	20010831		
	US 2003-404716	B1	20030401		

OS MARPAT 139:133836
GI



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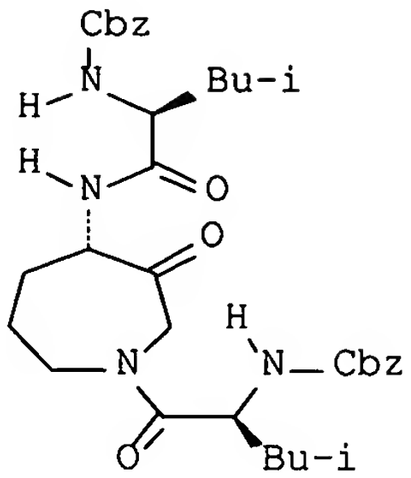


II

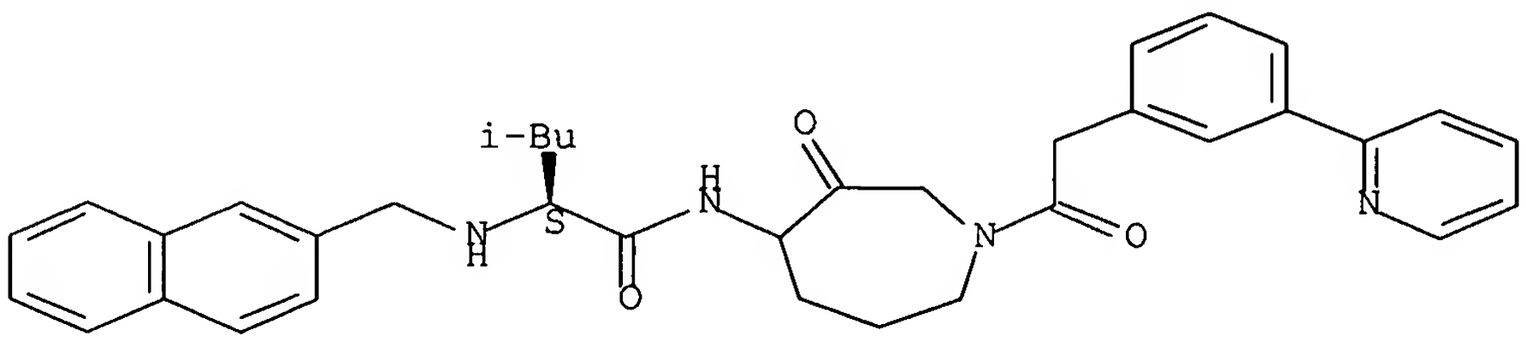
AB Aminoazepanones I [R1 = alkanoyl, amino-, alkoxy-, or alkylthioalkanoyl, etc.; R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, (thio)acyl, alkylsulfonyl, etc.; R3 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, etc.; R4 = H, alkyl, arylalkyl, etc.] or their pharmaceutically-acceptable salts were prepared as protease inhibitors, including cathepsin K, for treating diseases of excessive bone loss or cartilage or matrix degradation, gingival disease, arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease. Thus, compound II (Cbz = benzyloxycarbonyl) was prepared by a multistep procedure.

IT 281214-87-7P 281214-94-6P 281214-95-7P
281214-99-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(preparation of (acylamino)azepanones as protease inhibitors)

RN 281214-87-7 CAPLUS

CN Pentanamide, N-[hexahydro-3-oxo-1-[[3-(2-pyridinyl)phenyl]acetyl]-1H-azepin-4-yl]-4-methyl-2-[(2-naphthalenylmethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

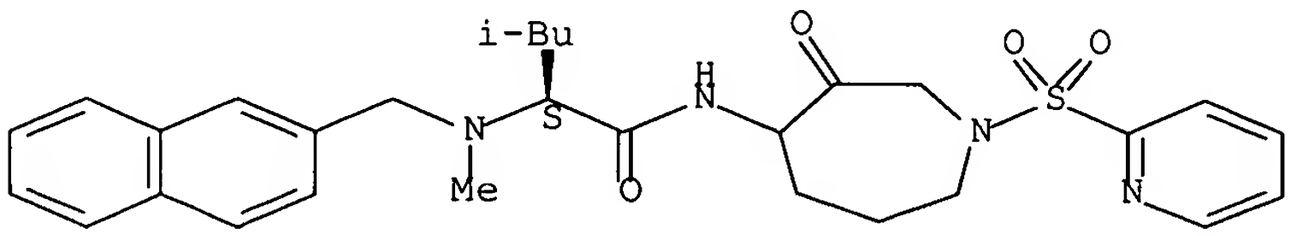
Absolute stereochemistry.



RN 281214-94-6 CAPLUS

CN Pentanamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[methyl(2-naphthalenylmethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

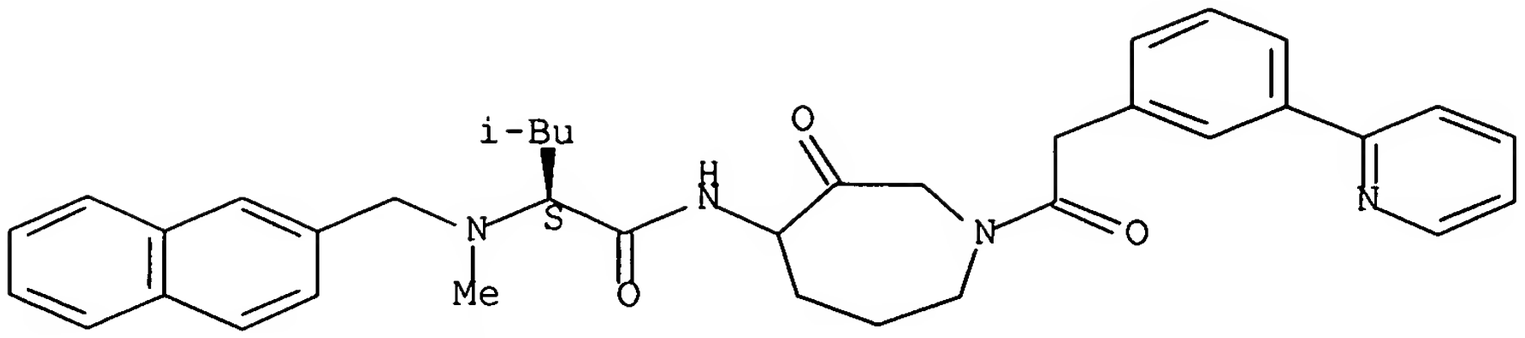
Absolute stereochemistry.



RN 281214-95-7 CAPLUS

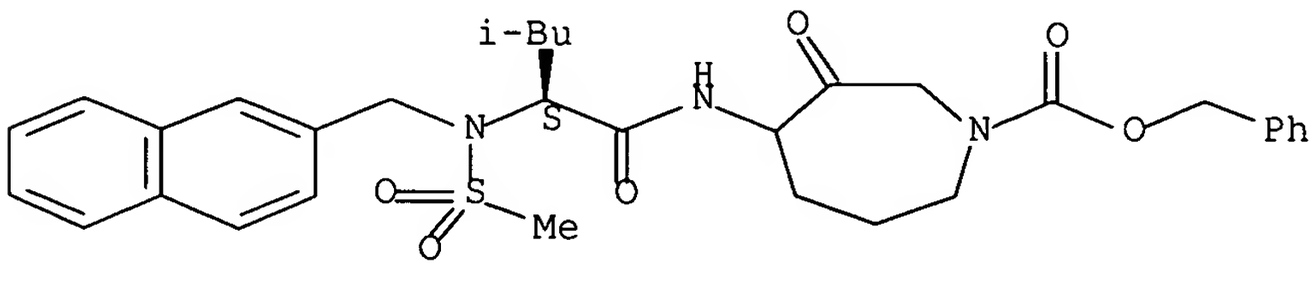
CN Pentanamide, N-[hexahydro-3-oxo-1-[[3-(2-pyridinyl)phenyl]acetyl]-1H-azepin-4-yl]-4-methyl-2-[methyl(2-naphthalenylmethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281214-99-1 CAPLUS
CN 1H-Azepine-1-carboxylic acid, hexahydro-4-[[(2S)-4-methyl-2-[(methylsulfonyl)(2-naphthalenylmethyl)amino]-1-oxopentyl]amino]-3-oxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:923616 CAPLUS Full-text
DN 136:53691
TI Preparation of 4-amino-azepan-3-one protease inhibitors
IN Marquis, Robert W., Jr.; Ru, Yu; Veber, Daniel F.; Cummings, Maxwell D.; Thompson, Scott K.; Yamashita, Dennis
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 322 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

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	BG 107327	A	20030731	BG 2002-107327	20021128
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	ZA 2002009808	A	20040709	ZA 2002-9808	20021203
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OS MARPAT 136:53691
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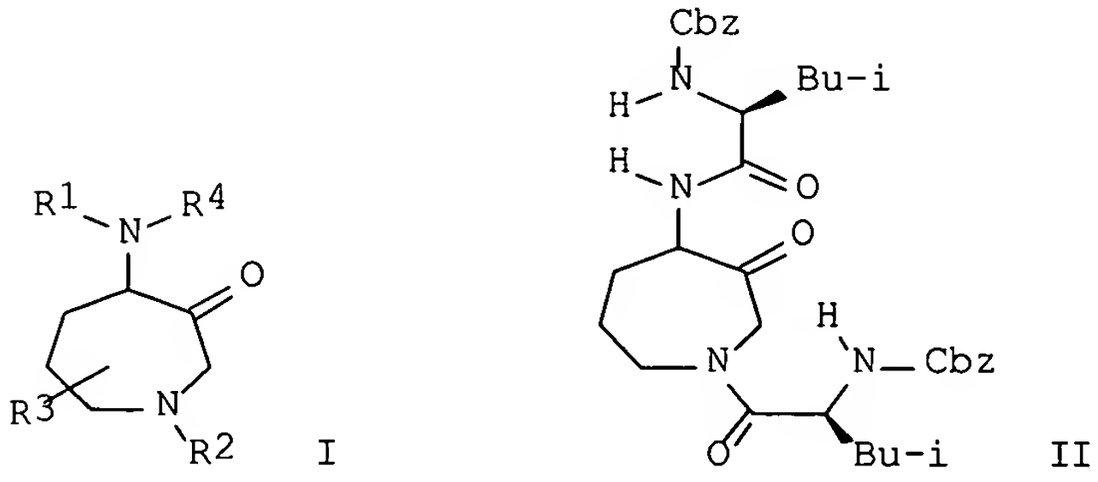


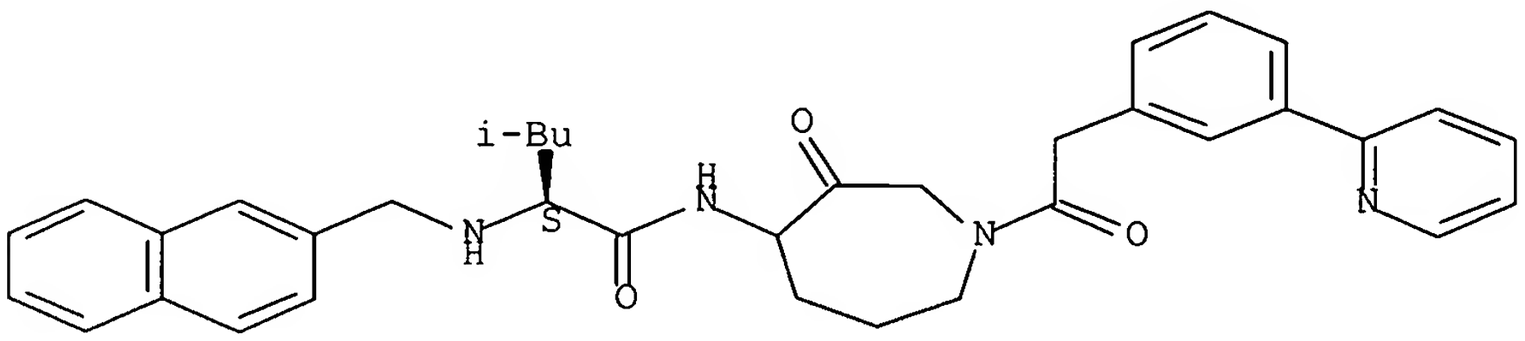
AB The title compds. [I; R1 = COCR13NR11R12, COCR13XR15, COCH2R13; R2 = H, alkyl, cycloalkylalkyl, etc.; R3 = H, alkyl, cycloalkylalkyl, etc.; R4 = H, alkyl, arylalkyl, etc.; R11 = H, alkyl, arylalkyl, etc.; R12 = H, alkyl, cycloalkyl, etc.; R13 = H, alkyl, alkenyl, etc.; R15 = H, alkyl, alkenyl, etc.] which inhibit proteases (no data), including cathepsin K, and are useful for treating diseases of excessive bone loss or cartilage or matrix degradation including osteoporosis, gingival disease including gingivitis and periodontitis, arthritis, more specifically, osteoarthritis and rheumatoid arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease, were prepared E.g., a multi-step synthesis of compound II was given.

IT 281214-87-7P 281214-94-6P 281214-95-7P
281214-99-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(preparation of 4-amino-azepan-3-one protease inhibitors)

RN 281214-87-7 CAPLUS

CN Pentanamide, N-[hexahydro-3-oxo-1-[[3-(2-pyridinyl)phenyl]acetyl]-1H-azepin-4-yl]-4-methyl-2-[(2-naphthalenylmethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

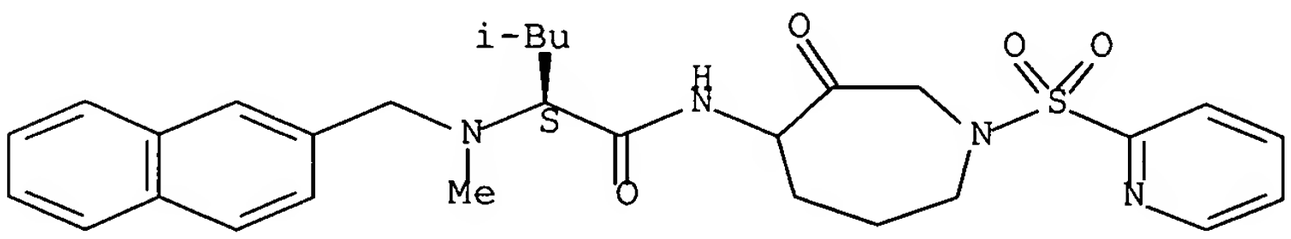
Absolute stereochemistry.



RN 281214-94-6 CAPLUS

CN Pentanamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[methyl(2-naphthalenylmethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

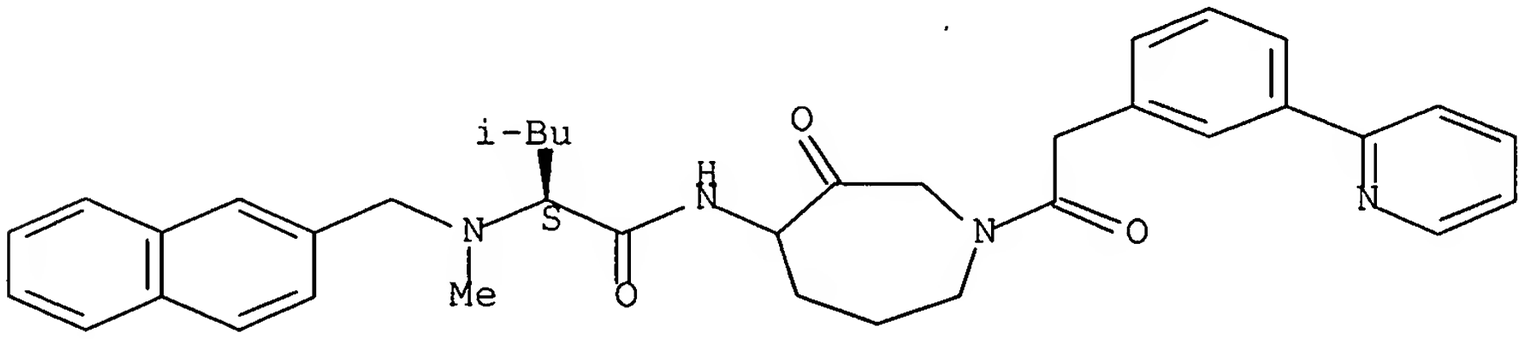
Absolute stereochemistry.



RN 281214-95-7 CAPLUS

CN Pentanamide, N-[hexahydro-3-oxo-1-[[3-(2-pyridinyl)phenyl]acetyl]-1H-azepin-4-yl]-4-methyl-2-[methyl(2-naphthalenylmethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

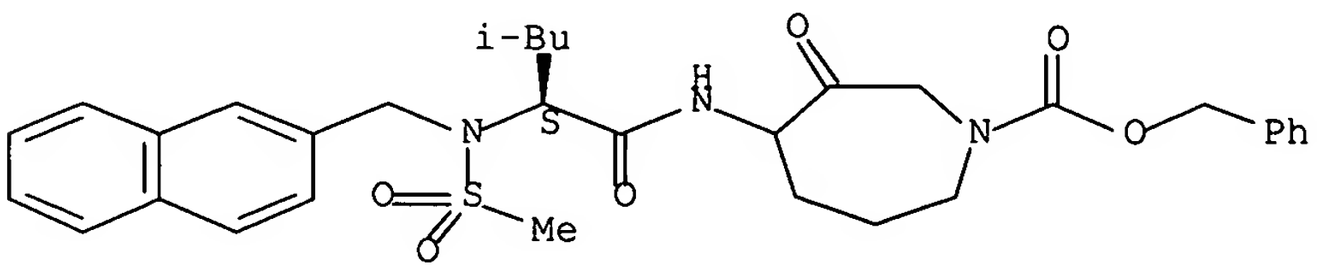
Absolute stereochemistry.



RN 281214-99-1 CAPLUS

CN 1H-Azepine-1-carboxylic acid, hexahydro-4-[[(2S)-4-methyl-2-[(methylsulfonyl)(2-naphthalenylmethyl)amino]-1-oxopentyl]amino]-3-oxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:456887 CAPLUS Full-text
DN 133:89444
TI Preparation of 4-amino-azepan-3-one protease inhibitors
IN Marquis, Robert Wells, Jr.; Ru, Yu; Veber, Daniel Frank; Cummings, Maxwell David; Thompson, Scott Kevin; Yamashita, Dennis
PA Smithkline Beecham Corp., USA
SO PCT Int. Appl., 273 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

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	US 2004002487	A1	20040101	US 2003-404716	20030401
	AU 2003261482	A1	20031204	AU 2003-261482	20031106
	US 2005256104	A1	20051117	US 2005-152745	20050614
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	US 1999-164581P	P	19991110		
	AU 2000-19411	A3	19991221		
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OS MARPAT 133:89444
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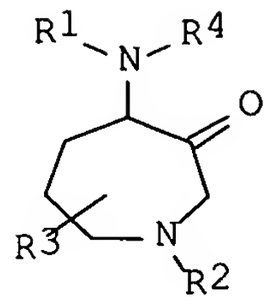

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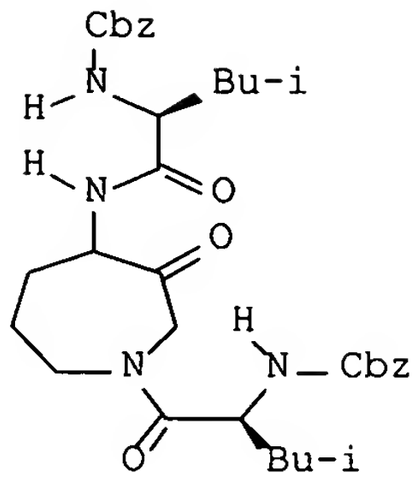


II

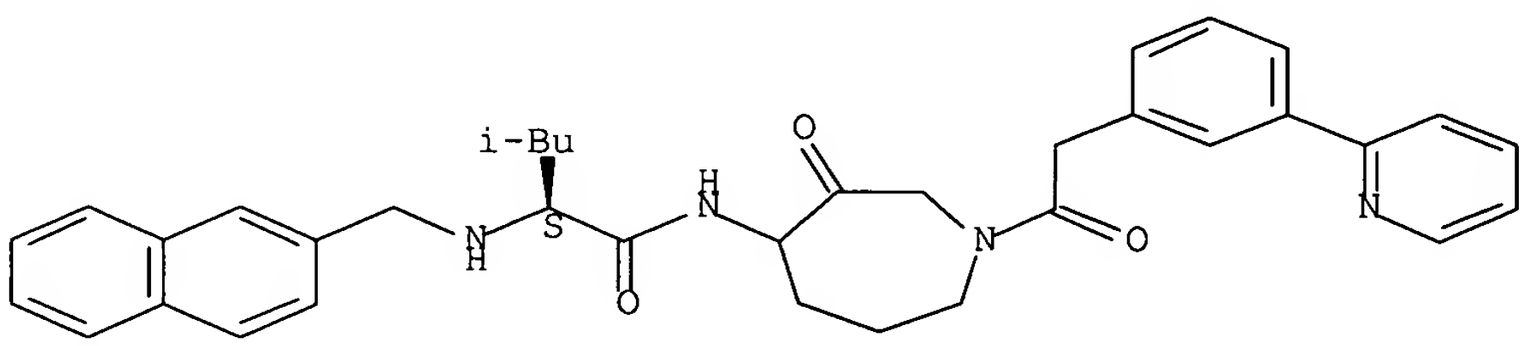
AB The title compds. [I; R1 = COCR13NR11R12, COCR13XR15, COCH2R13; R2 = H, alkyl, cycloalkylalkyl, etc.; R3 = H, alkyl, cycloalkylalkyl, etc.; R4 = H, alkyl, arylalkyl, etc.; R11 = H, alkyl, arylalkyl, etc.; R12 = H, alkyl, cycloalkyl, etc.; R13 = H, alkyl, alkenyl, etc.; R15 = H, alkyl, alkenyl, etc.] which inhibit proteases (no data), including cathepsin K, and are useful for treating diseases of excessive bone loss or cartilage or matrix degradation including osteoporosis, gingival disease including gingivitis and periodontitis, arthritis, more specifically, osteoarthritis and rheumatoid arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease, were prepared E.g., a multi-step synthesis of compound II was given. Compds. I are effective at 0.4-400 mg/kg/day.

IT 281214-87-7P 281214-94-6P 281214-95-7P
281214-99-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-amino-azepan-3-one protease inhibitors)

RN 281214-87-7 CAPLUS

CN Pentanamide, N-[hexahydro-3-oxo-1-[[3-(2-pyridinyl)phenyl]acetyl]-1H-azepin-4-yl]-4-methyl-2-[(2-naphthalenylmethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

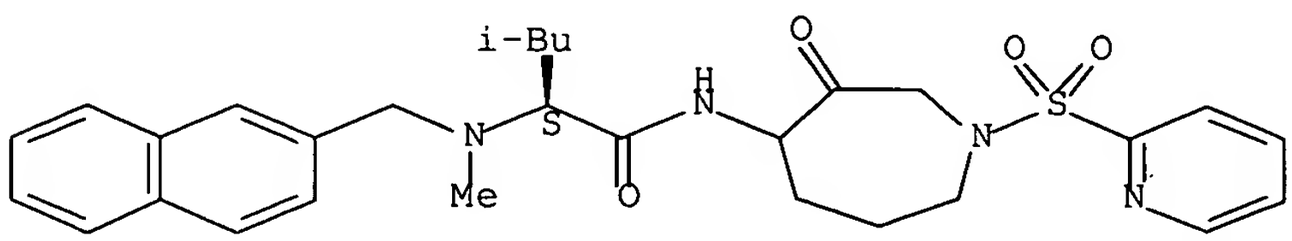
Absolute stereochemistry.



RN 281214-94-6 CAPLUS

CN Pentanamide, N-[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-2-[methyl(2-naphthalenylmethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

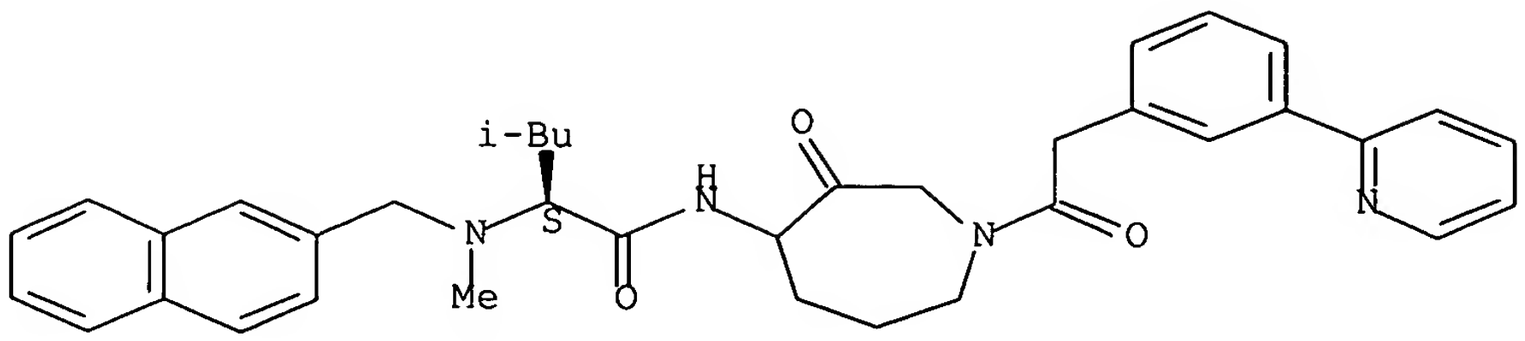
Absolute stereochemistry.



RN 281214-95-7 CAPLUS

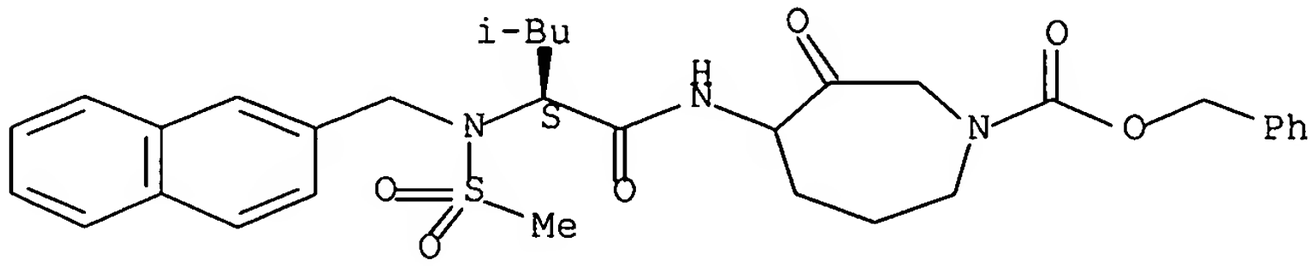
CN Pentanamide, N-[hexahydro-3-oxo-1-[[3-(2-pyridinyl)phenyl]acetyl]-1H-azepin-4-yl]-4-methyl-2-[methyl(2-naphthalenylmethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 281214-99-1 CAPLUS
CN 1H-Azepine-1-carboxylic acid, hexahydro-4-[[(2S)-4-methyl-2-[(methylsulfonyl)(2-naphthalenylmethyl)amino]-1-oxopentyl]amino]-3-oxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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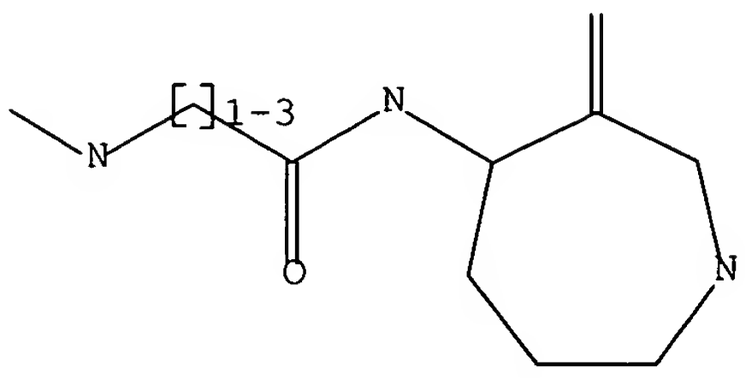


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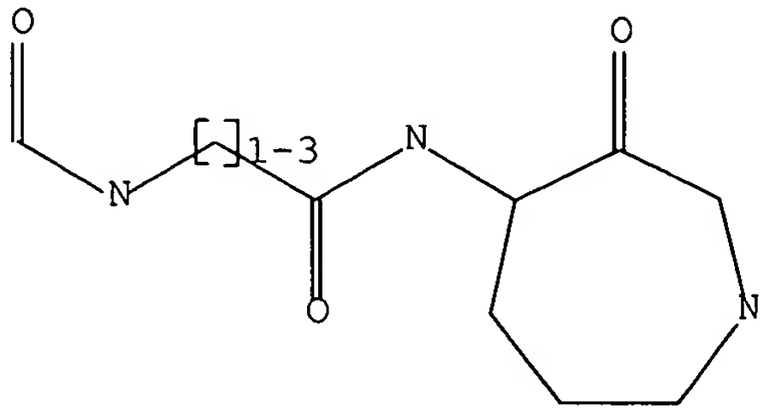


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L4                STRUCTURE UPLOADED
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L6           1039 S L4 FUL SUB=L3
L7             40 S L3 NOT L6

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L8              6 S L7


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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    31.58     241.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                    -4.50      -4.50

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